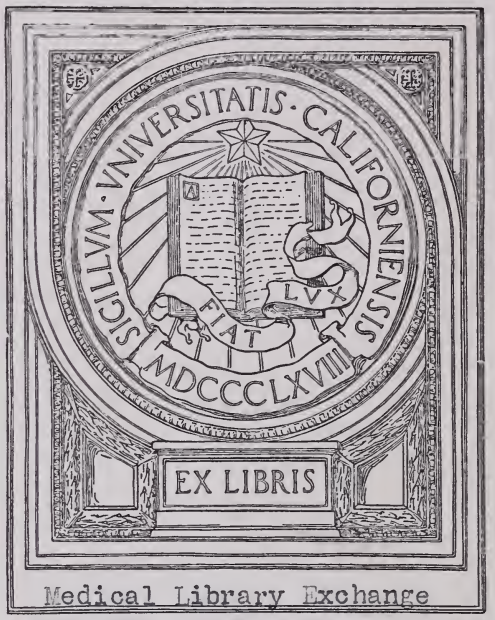
MEDICAL SCHOOL
LIBRARY



Medical Library Exchange

Northwestern University
Medical School Library

RADIUM REPORT
of the
MEMORIAL HOSPITAL

New York (City). Memorial Hospital

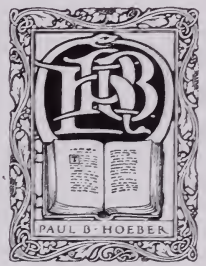
RADIUM REPORT

of the

MEMORIAL HOSPITAL

NEW YORK

[*SECOND SERIES*, 1923]



RC271
R3
N532r
v. 2
1924

PAUL B. HOEBER, INC.
NEW YORK · MCMXXIV

49386

Copyright, 1924
By PAUL B. HOEBER, Inc.

Published February, 1924

UNIV OF CALIF
MEDICAL SCHOOL

Printed in the United States of America

LIST OF CONTRIBUTORS

Bagg, Halsey J., Ph.D.
Associate in Biology, Memorial Hospital.

Bailey, Harold C., M.D.
Associate Professor of Obstetrics and Gynecology, Cornell University Medical College; Formerly Attending Gynecologist, Memorial Hospital.

Barringer, Benjamin S., M.D.
Attending Surgeon, Urological Department, Memorial Hospital.

Dean, Archie L., Jr., M.D.
Assistant Surgeon, Memorial Hospital.

Ewing, James, M.D.
Professor of Pathology, Cornell University Medical College; Pathologist, Memorial Hospital.

Healy, William P., M.D.
Attending Gynecologist, Memorial Hospital.

Janeway, H. H., M.D.
Late Attending Surgeon, Memorial Hospital.

Lee, Burton J., M.D.
Clinical Professor of Surgery, Cornell University Medical College; Attending Surgeon, Memorial Hospital.

Quick, Douglas, M.D.
Attending Surgeon, Memorial Hospital.

Quimby, Edith H., M.A.
Assistant Physicist, Memorial Hospital.

Stone, William S., M.D.
Clinical Director, Memorial Hospital.

CONTENTS

Chapter		Page
I.	The Present Status and Scope of Radium Therapy at the Memorial Hospital. . . . . *By H. H. Janeway*	1
II.	Technical Principles Employed in Radium Therapy at the Memorial Hospital. . . . . *By H. H. Janeway*	5
III.	Malignant Tumors of the Intraoral Group. . . . . *By Douglas Quick*	31
IV.	Carcinoma of the Rectum. . . . . *By Douglas Quick*	82
V.	New Growths of the Parotid Gland . . . *By Douglas Quick*	93
VI.	New Growths of the Eyeball and Orbit . *By Douglas Quick*	95
VII.	Malignant Tumors of the Skin. . . . . *By Douglas Quick*	97
VIII.	The Use of Radium in Cancer of the Female Generative Organs . . . . . *By Harold Bailey and Edith Quimby*	108
IX.	Vulval and Vaginal Cancer Treated by Filtered and Unfiltered Radium Emanation . . . . . *By Harold Bailey and Halsey J. Bagg*	129
X.	Follow-up Results of 908 Cases of Uterine Cancer Treated by Radium. . . . . *By Harold Bailey and William P. Healy*	138
XI.	Technique and Results in the Treatment of Carcinoma of the Breast by Radiation. . . . . *By Burton J. Lee*	145
XII.	Treatment of Recurrent Inoperable Carcinoma of the Breast by Radium and Roentgen Rays . *By Burton J. Lee*	153
XIII.	Results of the Treatment by Radiation of Primary Inoperable Cancer of the Breast. . . . . *By Burton J. Lee*	162
XIV.	Carcinoma of the Prostate . . . *By Benjamin S. Barringer*	174
XV.	Radium Treatment of Carcinoma of the Bladder . . . . . *By Benjamin S. Barringer*	192
XVI.	Radium Therapy of Teratoid Tumors of the Testicle . . *By Benjamin S. Barringer and Archie L. Dean, Jr.*	213
XVII.	Epithelioma of the Penis. . . . . *By Benjamin S. Barringer and Archie L. Dean, Jr.*	220
XVIII.	The Present Field for the Use of the X-Rays and Radium in the Treatment of Malignant Tumors. . . . . *By William S. Stone*	232
XIX.	An Analysis of Radiation Therapy in Cancer. The Mütter Lecture. . . . . *By James Ewing*	243

LIST OF ILLUSTRATIONS

Figure		Page
1.	Series of tubes for insertion within the larynx	8
2.	Series of tubes for insertion in center of an esophageal lesion	9
3.	Series of tubes for insertion through a stenosing cancer of the rectum	10
4.	Series of tubes for insertion into the uterocervical canal	10
5.	Brass container for carrying emanation tubes in the radium pack	11
6.	Mold of a lesion of the lip made of dental modeling compound	11
7.	Opposite surface of mold shown in Figure 6	12
8.	Lesion from which the mold illustrated in Figures 6 and 7 was made	13
9.	Applicator in place over the lesion	14
10.	Unfiltered emanation tubes fastened to end of wooden spatula	15
11.	Capillary glass tubes and forceps	15
12.	Needle for inserting glass emanation tubes within tumor tissue	16
13.	Active deposit applicator	17
14.	Wooden box for emanation tubes	18
15.	Larger glass emanation tubes and silver containers	19
16.	All the metal tubes used for filtration	20
17, 18 and 19.	Roentgenograms showing shadows of bomb placed directly against lesion	112, 113, 114
20.	Diagrammatic horizontal cross-section of female pelvis	115
21.	Diagram of apparatus for measuring distribution of radiation	116
22, A and B.	Diagrams of curves showing distribution of radiation	117, 118
23.	Various forms of radium applicators	119
24.	Diagram showing distribution of radiation	120
25.	Diagram showing radium "bomb" and tubes	121
26.	Recurrence of inflammatory carcinoma	154
27.	Diffuse cutaneous metastases before irradiation	155
28.	Disappearance of cutaneous metastases following irradiation	156
29.	Granular degeneration of cell bodies	157
30.	Punch used for suprapubic removal of carcinomatous prostatic base	176
31.	Method of inserting bare tubes of radium into carcinomatous prostatic base	177
32.	Radium changes in epidermoid carcinoma of bladder	178
33.	Epidermoid carcinoma of bladder growing into prostate	178
34.	Radium effect in epidermoid carcinoma of bladder	179
35.	Method of burying radium emanation tubes	199
36.	Surface application of radium emanations to growth	200
37.	Burying radium emanation tubes by suprapubic cystotomy	201
38.	Use of special retractor in exposing carcinoma	202
39.	Teratoma testis	215
40.	Longitudinal section of gross specimen	216
41.	Plasma-cell reaction about island of infiltrating carcinoma of bladder	245
42.	Diffuse lymphocytic and plasma-cell reaction in endometrium	246

FIGURE PAGE
43. Lymphocytic and plasma-cell reaction in squamous carcinoma of cervix ... 248
44. Adenocarcinoma of rectum ... 249
45. Extensive hornification of squamous carcinoma ... 250
46. Cervical lymph-node invaded by squamous carcinoma of tongue ... 251
47. Squamous carcinoma in lymph-node ... 252
48. Squamous carcinoma in lymph-node ... 253
49. Hornification and desquamation of cells in squamous carcinoma in lymph-node ... 254
50. Mammary carcinoma treated with bare emanation tubes ... 255
51. Rat sarcoma treated by injection of radium deposit ... 256
52. Muscle tissue of rabbit ... 257
53. Reaction about emanation needle in brain tissue of dog ... 258
54. Mediastinal tumor before and after *x*-radiation ... 259
55. Periosteal osteogenic sarcoma before and after *x*-radiation ... 260

FOREWORD

The first Radium Report of the Memorial Hospital was issued in 1917 and covered the work of the two preceding years in radiation therapy.

Two main considerations have led to delay in issuing the second report. The foremost of these has resulted from the rather numerous changes in technical methods which were found necessary in the development of the work while the treatment of various forms of carcinoma was in the experimental stage. The second consideration was the great desirability of having a longer period of observation of cases treated before attempting to form judgments regarding the efficiency of the methods used.

Owing to present uncertainties in both these particulars, no mention is made in this report of several diseases the radiation treatment of which is at present occupying much of the attention of the medical staff. For the forms of carcinoma discussed in this second report it is the belief of the staff that no radical changes are likely soon to occur either in the methods employed or in the character of the results obtainable by radiation, and it is therefore thought best to issue the report at this time.

Several of the contributions included in the report, as well as many others by members of our hospital staff, have already been published in various medical journals where they have been accessible for one or more years. Others have been prepared especially for this publication.

For the use of illustrations as well as for the privilege of reprinting, acknowledgment is hereby made to the following journals: *American Journal of Obstetrics and Gynecology; American Journal of Roentgenology and Radium Therapy; Annals of Surgery; Journal of the American Medical Association; Journal of Urology; Surgery, Gynecology and Obstetrics; Transactions of the College of Physicians.*

I

THE PRESENT STATUS AND SCOPE OF RADIUM THERAPY AT THE MEMORIAL HOSPITAL[1]

H. H. Janeway, M.D.

In 1917 The Memorial Hospital published a report of its experience of the two preceding years in the treatment of new growths by radium. Since that time, methods formerly used have been modified, and new ones developed: chief among the latter is the embedding of practically unfiltered emanation within tumor tissue. This method has proved so valuable that it now replaces most of those formerly used for the treatment of lesions of the mucous membranes, and either replaces or combines with other methods in the treatment of many external tumors. During the past four years, well-supported conclusions regarding the method of choice for different lesions and regarding safe and efficient dosage have been reached. In other words, standards for treatment have been established which are reliable and are possibly a close approach to the best. Moreover, a knowledge of what can be accomplished by radium in the various forms and stages of malignant growths has been acquired, so that a very accurate prognosis can now be given at the outset of treatment. This knowledge was not acquired sufficiently early for its incorporation in the present publication in the form of records of apparently complete retrogressions. The period covered by this report, like that of the preceding one, has been a period of growth; an attempt to discover just what radium is able to accomplish in the cure of cancer; a period of development of methods and dosage; of determining what forms of cancer can be benefited by radium, and to what extent.

Most of the material with which we were at first obliged to work might be called the deadwood of other hospitals, neglected or unsuccessfully operated upon by various physi-

[1] This article was written by Dr. Janeway shortly before his death, and was later somewhat revised.

cians and surgeons. A report of percentages of cures upon material of this character is worthless. We now, however, have been able to establish certain standards with regard to those forms of cancer which can be cured, and at what advancement; also what methods and what dosage are efficient in our experience to date. In the future, cases can be intelligently classified at the beginning of treatment from a standpoint of prognosis, and a report made of the proportion in each class apparently cured or benefited.

The results of treatment of malignant growths by radium are largely dependent upon the method of application. For this reason, each one of these different methods may be regarded as a separate therapeutic agent. It is frequently stated in surgical literature regarding the management of malignant tumors of practically every variety, that radium has been tried and has failed. In the cases cited, the radium element in one or several tubes has usually been laid over the growth for different periods of time; but the results obtained do not represent its possibilities in the slightest degree.

By patient trial during the past six years of one method after another, of various forms of filtration, of different dosage, and finally, of buried emanation, the efficiency of the treatment of many forms of cancer has reached a stage at the Memorial Hospital which justifies the attending staff in turning over to radium treatment the operable as well as the inoperable varieties of many malignant tumors. The personnel of the attending staff insures a strong consideration from the surgical standpoint; and we believe that any outside difference of opinion depends largely upon the difference in results produced by various methods of treatment.

The varieties of cancer deemed appropriate for treatment include cancer of the skin, lip, nasal cavity, maxillary antrum, tongue, floor of the mouth and lower jaw, tonsil, esophagus, uterus, bladder, testes, many cancers of the larynx and rectum, and many varieties of sarcoma. Operable growths of the stomach and breast are still excised; but, with patients who refuse operation, the results on operable tumors of the breast obtained by radium alone or combined with *x*-rays, have been good enough to broaden greatly their use in this field. The treatment of operable

carcinoma of the larynx by radium is still questioned; but the concensus of opinion at the Memorial Hospital is that, considering the possible sacrifice of the larynx, the results already obtained by radium are sufficiently good to justify the trial of radium before laryngectomy. Many will also question, perhaps with justice, our broad use of radium in cancer of the rectum, believing that the results are insufficient to justify its use in operable rectal cancer. Here again, the frequent unfortunate consequences of operation, the possible loss of sphincter control or the need of an artificial anus have frequently been responsible for our choice of radium. The justification of the treatment by radium of early cancer of the remaining organs mentioned in the above list is not, we believe, open to question; and it is the object of the present report to furnish evidence for this and the other views stated above. As mentioned, this evidence cannot yet be based upon percentages of cures, but rather upon results in individual cases, as well as upon a certain regularity with which such results can be obtained.

Our view, we believe, is further substantiated by a comparison of radium successes and failures, on one hand, with the disabling deformities of surgical successes and the pitiable condition of surgical failures, on the other. This applies especially to cases on the borderline of operability. We are certain from our experience at the Memorial Hospital that the apparent irresponsibility and freedom with which attempts are made to excise cancer, too frequently render the disease almost immediately worse rather than better, and unfit it for treatment by radium, to which, after it is too late, it finally comes. In making these comparisons one important fact must be kept in mind, namely, that the end-results, whether secured by surgical or other treatment, depend more upon the type of growth than upon any other factor. This fact is well illustrated by the freedom from recurrence occasionally reported after gastrectomy for the removal of large growths of the stomach. It is well illustrated by cancer of the breast. Neither operation nor radium will save certain diffuse, rapidly growing, invasive carcinomas of the breast often occurring in young women, whether treated before axillary nodes are palpable or not.

The surgical cures are of the less invasive type which have remained longer localized. Although a very malignant tumor, epidermoid carcinoma possesses a strong tendency toward circumscribed growth; few cases develop metastases beyond the regional groups of lymphatics. It is for this reason, unquestionably, that radium so successfully manages these growths. The contrast presented by lymphosarcoma—a tumor most sensitive to radium, but one which rarely fails to kill by general metastases—strongly emphasizes the importance of the invasive character of a tumor in its prognosis. No well-informed surgeon would today operate on tumors having pronounced invasive tendencies. For the cure of these cases a general remedy must be awaited. At present, local relief from radium and *x*-rays is preferred; a relief which strengthens nature's barrier of lymphocytic infiltration, instead of sweeping it away by excision; and one which often proves surprisingly complete. With growths of a less invasive type, those, for instance, illustrated by the whole class of epidermoid carcinomas, records show that the vast majority of successful end-results were obtained by a local agent. Surgery is a local agent. Its results depend upon the localized character of the disease which it attacks. Only about 4 per cent of carcinomas of the breast, when attacked after the involvement of the axillary glands, remain well for any length of time; almost equally poor are the results after the glandular invasion in epidermoid cancer. It becomes apparent, therefore, that, apart from constitutional agents, the cure of carcinoma practically depends upon a local remedy, that is, a remedy applied sufficiently early at the primary seat of the disease. As a local remedy, radium, when successful, undeniably involves far less initial damage and far fewer permanent sacrifices than does the knife. Radium, moreover, by no means excludes, but rather enhances the efficiency of any attention necessary to the glands. It is of much importance, therefore, to call attention to what can be accomplished by its use—the object of the present report—and as early as possible to establish this information on the percentage basis used in surgical literature. Only in this way can the most efficient therapeutic measure, that best adapted to the good of the patient, be selected.

II

TECHNICAL PRINCIPLES EMPLOYED IN RADIUM THERAPY AT THE MEMORIAL HOSPITAL

H. H. Janeway, M.D.

A knowledge of the physics of radium is necessary for an understanding of the present methods of its application. This subject was explained in some detail by Dr. Failla in the preceding (1917) report from the Memorial Hospital.

In brief, radium is radioactive because it discharges at a constant rate alpha rays—positively charged atoms of the gas helium. By the loss of these helium atoms, the atoms of radium from which they come are no longer atoms of radium, but become transformed into atoms of the gas called radium emanation. But the atoms of the gas emanation also lose at a constant rate atoms of helium, and by this loss the emanation becomes again transformed into a metal. By similar changes this metal becomes transformed into six other metals, all of which, during the process of their formation, are mingled together, constituting a mixture named active deposit. From some of the elements constituting active deposit are given off alpha rays; but from others, especially from two of them, rays of a different type, the beta and gamma rays. It is, therefore, from the active deposit alone that the radiations of most therapeutic value are derived. The same therapeutic value may, in consequence, be derived from active deposit, as from the element radium; in fact, the therapeutic rays from radium element enclosed within a container, arise not from the radium element directly, but from the collecting active deposit. Inasmuch as both emanation and the active deposit derived from it together may be made to occupy a very much smaller space than the radium from which they are derived, and a space of any desired shape; and inasmuch as their activity when ripened equals that of the radium producing them, it

becomes evident that more advantages in the treatment of malignant new growths are obtained by the use of the disintegration products of radium than by the use of radium itself. These advantages are:

1. The use of emanation in radium applications precludes loss of any of the radium element by accident or theft.

2. Because of the small size of the capillary tubes containing the emanation, they may be more uniformly distributed over the surface or through the tissues of tumors than could tubes of radium element designed for general use and not adapted to each special case.

3. The small size of these tubes makes possible the use, for any degree of filtration desired, of smaller and more serviceable metal tubes than is possible with radium element.

4. Inasmuch as it is possible to collect daily from any quantity of radium sufficient emanation to equal, when combined with the emanation previously collected and still available for use, an activity of about 90 per cent of the total quantity of radium supplying the emanation, a negligible loss of the total activity is involved in obtaining this activity from the emanation instead of from the radium element; a loss more than compensated for by the greater economy as well as the greater efficiency coming from the other mentioned advantages of the use of emanation instead of radium.

It must not be forgotten, in the use of emanation for therapeutic purposes, as is also the case with the radium element, that the real source of the radiations is the active deposit formed from the emanation upon the inside surface of the glass tube enclosing it. As it is possible to separate emanation from radium, it is also possible to separate the active deposit itself from the emanation. Though emanation is best adapted for the majority of therapeutic purposes for which radium radiations are of value, there are at present few conditions in which the active deposit alone is used to advantage. The therapeutic field of isolated active deposit will grow.

Active deposit may be collected on the surface of lead-foil, 0.1 mm. thick, folded on the inside surface of a glass tube, into which purified emanation may be forced. After the

surface of the lead has become coated with the active deposit, the emanation may be withdrawn for other uses, the glass tube broken and the lead foil used for certain superficial lesions, such as vernal catarrh and nevi; lesions for which applications of this kind are of special value.

Active deposit may be collected from emanation on sodium chloride, the emanation drawn off and preserved for other uses, and the salt dissolved in water. The solution, then, may be injected intravenously in certain conditions in which it is of value. Active deposit used in this way makes radium a constitutional agent.

At the Memorial Hospital radium element is seldom used; but only its disintegration product, active deposit, which gives off directly the rays of therapeutic value. This active deposit may be either that which coats the interior of sealed capillary glass tubes containing emanation which replenishes the active deposit until the emanation is exhausted, or it may be the active deposit separated from its mother, emanation, and depending for the duration of its activity upon its own length of life.

Active deposit decays far more rapidly than emanation, diminishing to one-half its original strength in roughly one-half an hour. Emanation, on the other hand, decreases to one-half its original quantity in about four days. For this reason sealed glass tubes containing definite quantities of emanation possess a wider range of therapeutic usefulness than the rapidly disintegrating active deposit. Experience has demonstrated that the mild, prolonged action of the encapsulated emanation is more effective upon malignant tissue than the more intense and brief action of isolated active deposit. Economical considerations, depending upon the collection of active deposit, and practical ones concerning its use are other factors which may later be eliminated.

METHODS OF RADIUM APPLICATION

The introduction, since the publication of the last report, of the use of buried emanation has eliminated many of the methods suggested in that report for the application of radium to the surface of new growths. The present technique includes mainly the following six methods of application:

1. The use of one or of several metal tubes, linearly arranged, filtering their contained capillary glass emanation tubes and themselves contained inside one end of a long rubber tube. Such tubes are used in the interior of a growth which infiltrates the walls of a hollow viscus, projecting into and more or less obstructing its lumen; as in growths of the

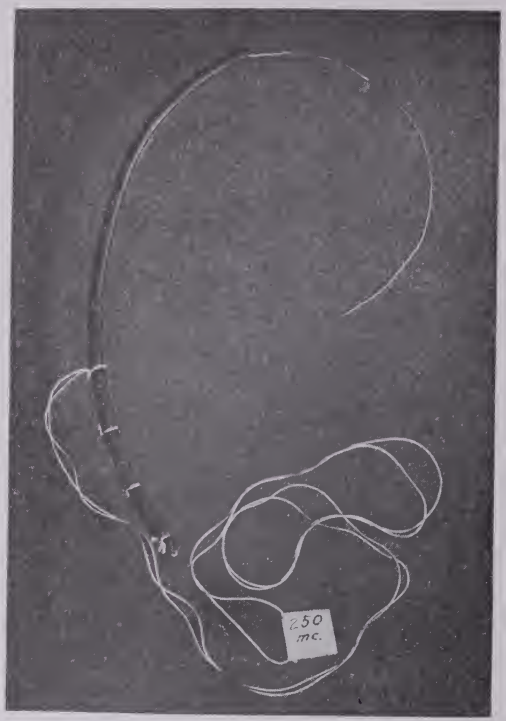


FIG. 1. Series of tubes tied in a long rubber tube for insertion within the larynx. The protruding wire passes through the whole length of the applicator. It is very flexible, but adds sufficient rigidity to the applicator to facilitate its insertion and maintain it in position.

larynx, esophagus, rectum or cervix uteri (Figs. 1, 2, 3 and 4).

2. The use of many 0.5 mm. silver tubes, containing glass emanation tubes, evenly distributed over the floor of a circular brass tray, 6 cm. in diameter and fastened to this floor by paraffin; or distributed over the floor of a rectangular

box 7 × 10 cm., to which floor the tubes are held in place between pegs. Lead was formerly used to line these floors, but is now replaced by brass of desired thickness. Such applicators are used at a distance from the surface over deeply situated growths (Fig. 5).

3. The use of metal tubes, containing emanation tubes, evenly distributed within the substance of a mold of the

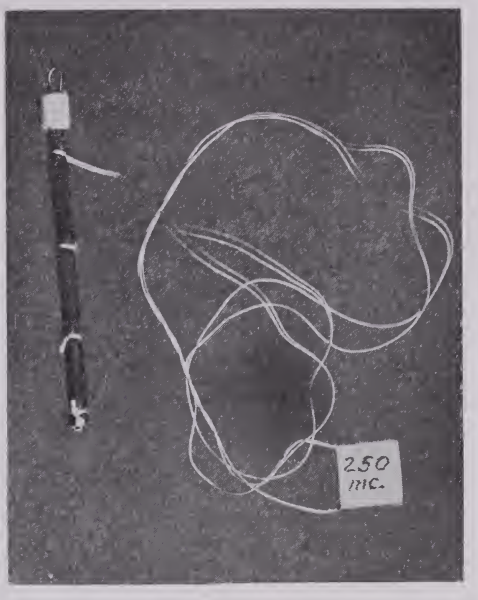


Fig. 2. Series of tubes tied in a short rubber tube, rendered more rigid by a wire, for insertion in the center of an esophageal lesion. Sometimes these applicators may be inserted from above with the aid of the esophagoscope. At other times they must be pulled into place by a string, which has been previously swallowed and delivered through a gastrostomy opening.

The enlargement at one end produced by wrapping adhesive around the applicator stops the applicator when it is pulled through the stenosis at the correct level.

lesion made of a dental modeling compound. This compound softens to a pliable consistency when warmed in hot water, but is hard at ordinary or even body temperatures (Figs. 6, 7, 8 and 9).

4. The use of applicators made by fastening unfiltered emanation tubes closely together with paraffin upon the end

of a wooden spatula, thus permitting unfiltered emanation (active deposit) to be applied absolutely uniformly and close to the surface of the lesion (Fig. 10).

5. Embedding emanation, sealed in capillary glass tubes, throughout the substance of tumor tissue (Figs. 11 and 12).

Fig. 3.

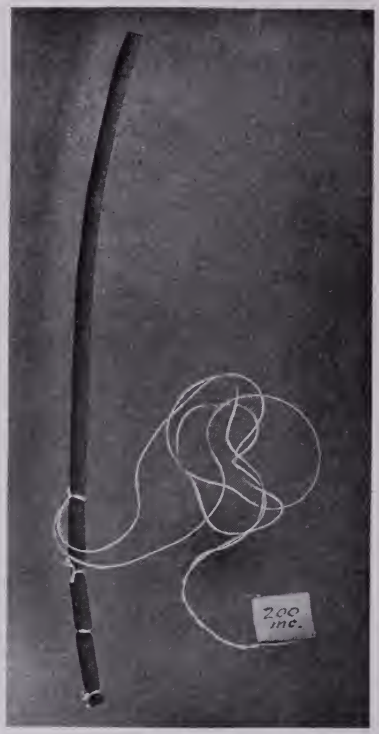


Fig. 4.

Fig. 3. Series of tubes tied in one end of two long rubber tubes, one inside of the other, for insertion through a stenosing cancer of the rectum. The applicator is given the rigidity of a bougie by the use of two tubes instead of one for enclosing the metal tubes. The long end protrudes through the arms, and prevents misplacement of the applicator, when fastened externally by adhesive plaster.

Fig. 4. Series of tubes tied inside a long rubber tube for insertion into the uterocervical canal.

6. Close-surface application of active deposit evenly collected upon the surface of small thin lead sheets (Fig. 13).

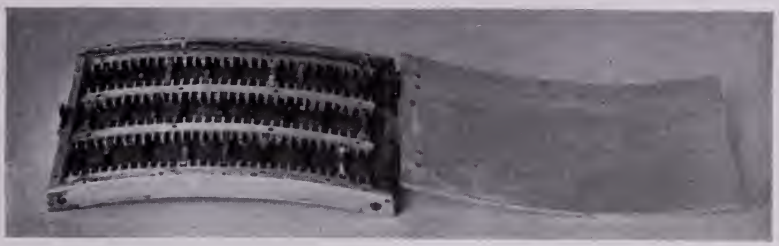


FIG. 5. Brass container for carrying emanation tubes in the radium pack.

FIG. 6. A mold of a lesion of the lip (Fig. 8) made of dental modeling compound. The surface of the mold represented in this figure fits over the lesion, and illustrates the tubes buried within it, which filter and enclose the emanation.

"Tubes" is a term meaning capillary glass tubes, 0.6 mm. in diameter, 10 to 15 mm. long, within which is sealed the gaseous emanation, these tubes being themselves enclosed in metal tubes furnishing the desired filtration. At the Memorial Hospital the emanation is also collected in small

FIG. 7. Opposite surface of the mold shown in Figure 6. It illustrates the indentations made by the patient's teeth which hold the applicator in place.

capillary glass tubes, 0.3 mm. in diameter, 3 mm. long, for use according to Method 5.

It is important as soon as these tubes ripen (a process practically complete in three hours) to know the exact amount of emanation which they contain. This is measured,

in the case of the longer glass tube, by its discharging effect upon an electroscope; and, in the case of the smaller glass tube, by means of a special ionization chamber, in series with a sensitive galvanometer. Once measured, the future strengths of these tubes is also known, provided they are kept isolated from each other; because their decay is at a constant rate, each tube becoming approximately 15 per cent weaker during each successive twenty-four hours. Isolation of the smaller tubes for embedding purposes is

FIG. 8. Lesion from which the mold, illustrated in Figures 6 and 7, was made.

obtained by grouping them in subdivisions in a wooden box (Fig. 14). More exact information regarding their production and measurement is given in the article by Dr. Failla, "Radium Technique at the Memorial Hospital," in *Archives of Radiology and Electrotherapy* for June, 1920.

Inasmuch as the smaller tubes above referred to are generally used on the day of collection, their history is quickly disposed of. It is, however, quite different with the longer tubes, which contain much more emanation, are repeatedly used in various applicators and on a number of patients, and are differently filtered. Each of these tubes, as soon as it is measured, must be kept isolated from its fellows—an isolation which must be maintained from

applicator to applicator, and from patient to patient. This isolation is usually accomplished by enclosing the emanation tubes in 0.5 mm. silver tubes which are enamelled in one, two, or three colors (Fig. 15). By these colors, different for every tube, each tube may be identified at a glance

FIG. 9. The applicator illustrated in Figures 6 and 7 in place over the lesion illustrated in Figure 8.

during the whole of its subsequent period of usefulness. Other emanation tubes enclosed in platinum or aluminum containers (filters relatively seldom used) are identified by these containers themselves. It is possible to enclose the great bulk of the longer glass emanation tubes within these

silver tubes, because 0.5 mm. silver forms the routine filter for close superficial application, and can be used as

FIG. 10.—Unfiltered emanation tubes fastened by paraffin to the end of a wooden spatula.

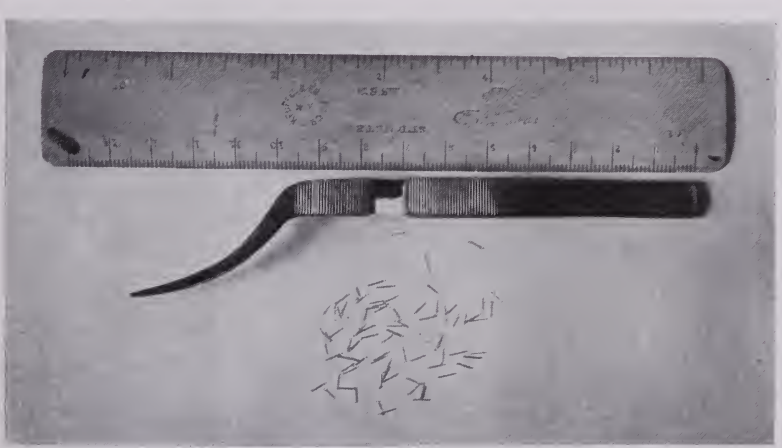


FIG. 11. Capillary glass tubes containing emanation and used for burying the emanation within the tumor tissue. Forceps used for handling these tubes.

part of the filter for deep therapy. Therefore, for all distant surface applications, it is unnecessary to empty the silver

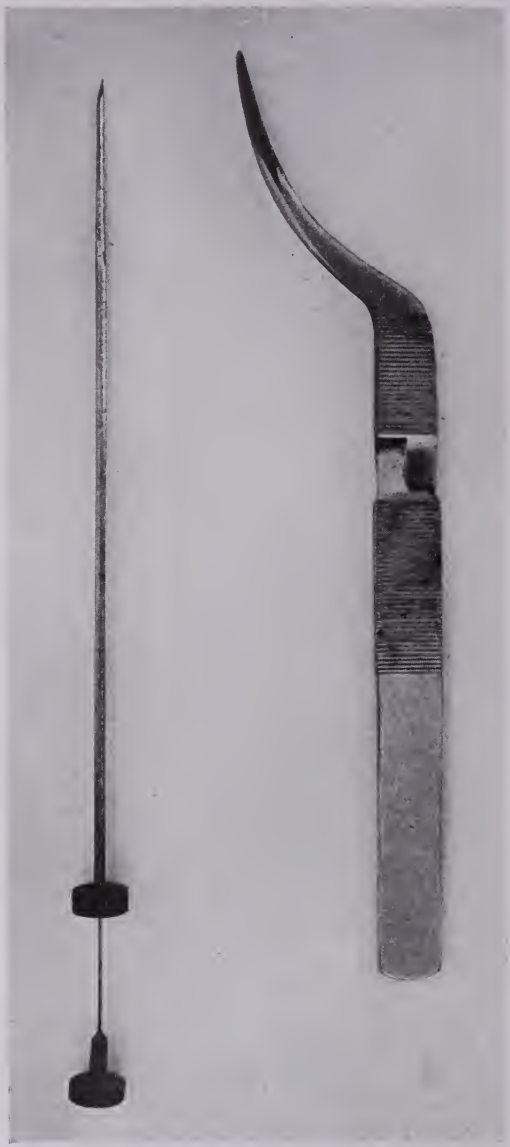


FIG. 12. Needle used for inserting the glass emanation tubes within the tumor tissue. Forceps for loading the needle.

tube in order to transfer its contents to the surface of 2 mm. of brass, the filter used in the distant applicators illustrated in Figure 5.

Filtration and Dosage. The purpose of filtering radium is to render uniform the dose of the radiations throughout the whole of the lesion treated. In the case of deeply situated lesions, it is necessary to diminish the difference between the dose received by the skin and layers of normal tissue overlying the tumor and that reaching the different depths of the tumor. Increasing the distance of the radium applicator

FIG. 13. Active deposit applicator. The single sheet of lead has deposited upon one surface practically all of the active deposit. This sheet is enclosed by folding over it the two sheets hinged together. When the active sheet is thus enclosed and the active surface laid against the lesion, this surface is filtered by one sheet of 0.1 mm. of lead, while the tissues opposite the lesion are protected by 0.2 mm. of lead.

as far as practical from the surface aids in accomplishing the same object. If it were possible to expose every layer of cancer tissue to the same quantity of radiations appropriate for the most superficial layer, the technique of radium applications would be easy. Unfortunately the dose safe for the skin differs little from that fatal to only the most superficial layers of the cancer. According to Schmitz the ratio is 2:1. According to Kroenig and Friedrich it is 170:150. In any case this ratio only too quickly changes by absorption when the safe skin dose is compared with the dose fatal to the

FIG. 14. Wooden box with hemispherical pockets for conveying and keeping emanation tubes.

deep cancer cells. In our experience the absorptive power of the superficial layers of tissue over the deepest cancer cells of even still localized growths, though such cells are buried only perhaps two centimeters, is great enough, in most locations in the body, to make it impractical to kill these cells by surface applications alone. Such surface applications will greatly assist other methods of treatment, even without the latter producing complete disappearance of the more susceptible tumors or much improvement in the more resistant types of growth.

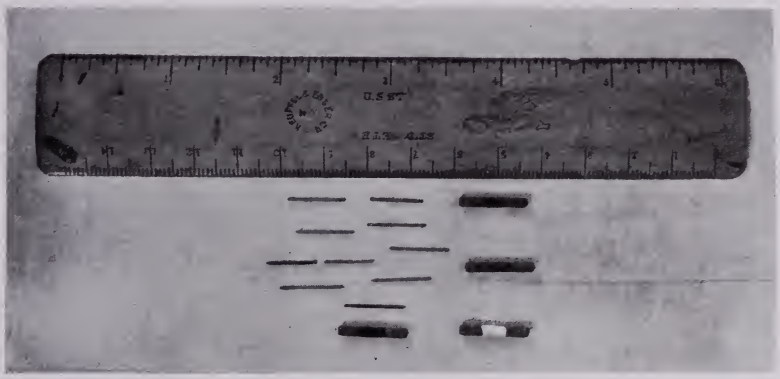


FIG. 15. Larger glass emanation tubes and their silver containers.

UNFILTERED RADIUM

Where no filtration at all is desired, the tissues are exposed to uncovered or "bare" emanation tubes, or to such tubes covered, merely for protection, by thin aluminum. The glass of the capillary tubes, in which the emanation is collected, filters out only the alpha rays but constitutes practically no filter to the beta and gamma rays, which alone are of therapeutic value in all surface applications. These tubes, therefore, are serviceable where no filtration is desired; and, aside from those made for embedding in cancer tissue, are most useful for very superficial lesions, especially nevi. The most suitable method of applying these tubes to surface lesions is by the applicator described under

Method 1. Because of the absence of filtration, the time of applications by this method is short, a great advantage in the treatment of nevi in children. The area covered on the end of one of these applicators is approximately 3 sq. cm., and the dosage at the distance from the skin (5 mm.) at which the tubes on these applicators are applied, is 10 mc. hrs. When wide areas are covered, these applicators must be

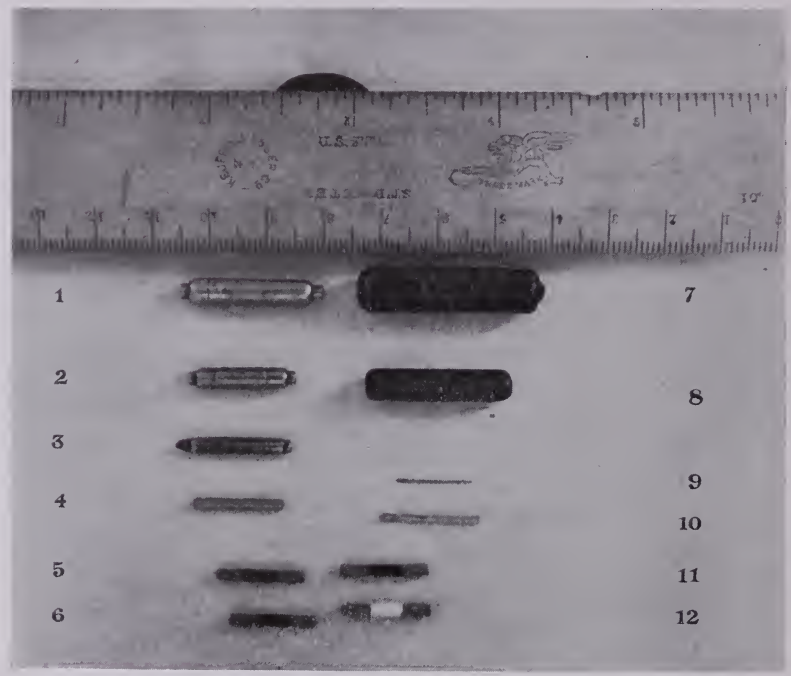


Fig. 16. All the metal tubes used for filtration.

1. 1½ mm. platinum tube seldom used now. 2. 1 mm. platinum tube. 3. 1 mm. platinum tube. 4. ½ mm. platinum tube. 5, 6, 11 and 12. ½ mm. silver tubes enamelled in three colors. 7. 3 mm. lead tube seldom used. 8. 2 mm. lead tube. 9. Tiny emanation tube for insertion into any of these metal tubes, which furnishes the desired filtration.

adapted carefully to the shape of the lesion; and much caution exercised by exact inking of the skin, not only to avoid overlapping of treated areas, but also to prevent cross-firing at the margins of treated areas.

The tubes of aluminum, having walls 0.2 mm. thick, within which the capillary glass emanation tubes are inserted for protection, are illustrated by Figure 16. The additional filtration offered by these aluminum tubes is unimportant. They are used to protect the emanation tubes, when using the latter without additional filtration where they are likely to be broken. Such applications are sometimes made over large, superficial or irregular lesions which it is desirable to cover with one applicator. The best way of covering them is by means of a mold of the lesion made of dental modeling compound. The lesion is then outlined with ink-dots upon the skin surface. In replacing the mold, the ink-marks will indicate upon it the contour of the lesion. Within such an outlined area the desired number of aluminum tubes, containing the emanation tubes, may be sunk into the mold. This is accomplished by making a groove for the tube in the mold with hot wire, one end of which (as long as the length of the tube) is bent at a right angle. The tube is then laid in its groove and retained in place by pouring liquid paraffin over it. This quickly hardens. The deeper the tubes are sunk, the greater the cross-fire between them and the fewer the tubes needed. By this method larger areas may be covered in a single application than is possible when uncovered emanation tubes, arranged close to each other, are used. A uniform action over the whole area is obtained in this way. In certain tumors, especially antral tumors, it is desirable to insert practically unfiltered emanation within the center of the tumor for definite lengths of time. Emanation tubes, protected by enclosure in thin aluminum ones, serve this purpose well. For lesions in which embedded emanation alone is not appropriate, filtration through platinum better meets the requirements.

For filtration the following metals are almost exclusively used at the Memorial Hospital:

1. Lead..... 0.1 mm. thick
2. Silver..... 0.5 mm. thick
3. Brass..... 2.0 mm. thick or its equivalent
4. Platinum . 0.4, 0.5 or 1 mm. thick

LEAD FILTRATION

Lead is the most useful filter and support for active deposit, especially for use in the conjunctival sac. It is easily bent and molded, and forms also an ideal increment to many applicators more lightly filtered or without filtration.

SILVER FILTRATION

Silver absorbs all but the hardest beta rays and many of the weakest gamma rays. It thus separates the softest radiations from the more penetrating ones. This filter is always used in the form of tubes, illustrated in Figures 15 and 16, and is the most widely used container at the Memorial Hospital for the longer glass emanation tubes. All superficial close applications to epithelioma are accomplished through this filter, usually by embedding the silver tubes at a depth of 3 mm. within molds of the lesion made of dental modeling compound, as above described.

The compound is ideally adapted for this purpose. When softened by warm water, it can be placed without discomfort over any lesion—for instance, within the mouth; and reproduces with accuracy a mold of the lesion. It hardens quickly, and the uneven indentations and elevations of the lesion are made clear; its boundaries are easily recognized, and may be outlined in ink; and the tubes containing the emanation, after being embedded within this marked area, will be accurately distributed over the lesion, when the mold is replaced upon it. The method is most useful and efficient for close surface application. A convenient modification of the same for small epitheliomas of the skin, especially those of the face, is made by placing the warm dental compound over the growth; and then, before the compound softens, sinking one (or more) silver tubes into its outside surface, until the tube is about 3 mm. distant from the lesion. The dental compound hardens and remains adherent to the skin, and also to the tube; so that, without adhesive plaster or other aid, the tubes are retained in place over the lesion for the desired time of the application. Such methods are especially useful near the hair margin, and around the nose, mouth and ears. To insure accuracy in applying the tubes

over the lesion, four ink lines, radiating at equal distances from the center of the tumor, are drawn around the growth before its location is hidden by the mold. When single tubes are used in this manner over superficial epitheliomas, the dose is 75 mc. hrs. per sq. cm. When larger areas (4 to 5 cm. in diameter) are covered, the dose must be reduced, because of cross-firing, to 60 mc. hrs. per sq. cm.; for still larger areas (8 cm. in diameter) to 50 mc. hrs. per sq. cm.; and for lesions 12 cm. in diameter, to 40 mc. hrs. per sq. cm.

Within the larynx close surface applications have been successfully administered by the use of one long silver tube, or two or three of regular size, according to the extent of the lesion. These are tied end to end within one extremity of a long rubber tube, after the manner of applicator No. 1. This tube may contain also a thin flexible wire, to give it rigidity. Such applicators may be inserted within the larynx under local anesthesia by means of special angular forceps, and may be held without displacement during a sufficient length of time to complete the application. By means of a mirror, accuracy of placement can be confirmed after insertion. Such an adjustment must be made as will bring the center of one tube—the upper when two tubes are used, the middle when three—opposite the lesion. This adjustment may be maintained through the whole time of treatment by the patient grasping between his teeth the end of the rubber tube which protrudes through his mouth.

The proper dose from such an applicator is 100 mc. hrs. per tube, when short tubes are used. For three tubes, therefore, the dose is 300 mc. hrs.; and for the long single tube, 200 mc. hrs.

In addition to the purpose served by these silver tubes for close application, their contained emanation may be transferred, as previously explained, to the heavily filtered surface application tubes—those designed especially for use at a distance from the surface.

These three functions consume the entire life of the vast majority of the longer glass emanation tubes; there are only a few other purposes for which it is desirable to use them. It is unnecessary, therefore, to remove these emanation tubes from their silver capsules until the serviceable period

of their disintegration is complete. Thus they are preserved from breakage, and, of more importance, from the necessity of remeasuring.

BRASS FILTRATION

Lead 2 mm. thick has been almost exclusively used for heavy surface filtration. The choice of this degree of filtration was justified by Rutherford's curve ("Radioactive Substances and their Radiations," p. 258). Recently Dr. Failla has plotted curves for the absorption by tissues. These curves show that 2 mm. of brass and 0.4 mm. of platinum supply all the filtration necessary to produce homogeneous radiations. The matter is detailed in Dr. Failla's paper. By the use of such filtration a strong dose can be administered at a far greater depth than without its aid; and, with the exception of the center of growths constricting the lumen of hollow viscera, where platinum is preferable, the filters of brass are limited almost exclusively to surface applications. In such use the brass filters are combined with additional filtration. This consists of the 0.5 mm. of silver in the tubes enclosing the emanation tubes, and also the material of which the applicators are made (in which brass is used) and finally the padding used to separate the applicators from the surface of the body. Altogether, this additional filtration is equivalent to 1 mm. of brass itself; so that, to secure a filtration equivalent to 2 mm. of brass in these surface brass applicators with which additional filtration is used, the brass in them must be only 1 mm. thick.

Inasmuch as greater depth of strong dosage, with diminishing damage to superficial tissues, can be proportionately increased by the greater distance from the surface at which these heavily filtered radium applicators are placed, the brass applicators are almost always used at a distance from the surface. Two distances have been found most practical: 3 cm., for which the circular tray is generally used, and 10 cm. for the rectangular box (Fig. 5). Superficial thick growths and those situated in the neighborhood of susceptible organs, such as the eye and thyroid, are treated at a distance of 3 cm., while deeply placed lesions, such as thoracic abdominal tumors, and bulky lymphatic glands are treated at

10 cm. The dose through 2 mm. of brass or its equivalent at 3 cm. from the surface is 2,250 to 2,800 mc. hrs., depending upon the condition of the tissues and the type of growth. At 10 cm., 18,000 to 21,000 mc. hrs. may be safely given at the first treatment. If it becomes necessary to repeat the treatment, the dosage must be diminished; as the superficial tissues are more sensitive unless long intervals—a year or more—have elapsed. The duration of similar exposures through 2 mm. of lead, formerly most frequently used, is 3,000 to 4,000 mc. hrs. at 3 cm. from the surface and 24,000 mc. hrs. at 10 cm. from the surface.

PLATINUM FILTRATION

Platinum is a very useful filter for a few lesions, namely, those for which tubes are desired. Because the filtration power of 1 mm. of platinum is equivalent to 2 mm. of lead, and 0.5 mm. of platinum is equivalent to 2 mm. of brass, platinum filters may be used to replace 2 mm. of lead or 2 mm. of brass, affording the advantage of much smaller tubes. Within stenosing lesions of the esophagus, rectum and uterocervical canal, rubber-covered tubes of 1 mm. platinum are easily inserted. Tubes of 0.5 mm. of platinum are more appropriate, being still smaller. The latter are often indispensable within the larynx. Though platinum filters have a limited field, within this field they cannot be replaced. Figure 16 illustrates the 1 mm. and 0.5 mm. platinum tubes used at the Memorial Hospital.

The correct dosage for emanation filtered by 1 mm. of platinum, placed in the center of stenosing lesions, depends upon the organ concerned. Within the larynx it should not be over 200 mc. hrs. per tube; within the esophagus, according to the extent of the lesion and consequent danger of perforation, 400 to 500 mc. hrs. per tube (three tubes being used); within the rectum, more than 400 or 500 mc. hrs. per tube is unwise; in the uterocervical canal as much as 1,000 mc. hrs. (three tubes being generally used) is not only sufficient, but also involves no unpleasant subsequent symptoms, even when combined, as in cervical cancer, with additional radiations from embedded emanation. The dosage through 0.5 mm. of platinum is 15 per cent less than

through 1 mm. of platinum, formerly most frequently used. With the exception of the larynx, the rubber-covered 1 mm. platinum tubes are conveniently fitted into stenosing lesions, as those of the esophagus, rectum and uterocervical canal. When the 0.5 platinum tubes are used in these locations, they may be covered with thick rubber so that the applis cator fits the canal snugly. Sometimes 2 mm. of brass tube-may be substituted.

THE METHOD OF BURIED EMANATION

Our final discussion is of treatment by unfiltered buried emanation, reserved to the last because of its importance. In perhaps no other method of applying radium are dosage and distribution of more importance. In our experience, the best end-results follow complete retrogression produced by one treatment. Probably the most important reason for this is the greater certainty of the complete disposal of the disease at an early stage, or before further extension from outlying remnants has had an opportunity to develop after incomplete destruction. In the case of radium therapy another factor unquestionably explains the better results from single treatments. Partially fibrosed tissues respond to radium less favorably than untreated tissues and with more discomfort to the patient, possibly because of their more indurated character, and less lymphocytic infiltration. An important factor, therefore, in success by radium therapy, is the selection of a safe and yet efficient dose for the first treatment; a dose producing as little caustic action as is consistent with complete destruction of the neoplasm. As already emphasized, in no method of treatment by radium is this selection of more importance than in the buried emanation method. Figure 11 shows the emanation tubes, in their natural size, used for embedding this gas, and Figure 12 the needle for inserting them into the tissue. The procedure is simple: a wire stylet of a needle is withdrawn a short distance from the point of the needle; the needle is then loaded through its pointed ends with one of the glass tubes, by means of a delicate forceps; it is then inserted into the substance of the tumor, and by means of the wire

stylet, the glass emanation tube is expelled. As even a distribution of these tubes as possible should be made throughout the whole tumor. This distribution depends, of course, upon the number of tubes used; and the number of tubes used depends quite as much upon the number possible to insert without danger to the patient, as upon how many millicuries each tube should theoretically contain. It should be the aim of treatment by buried emanation to produce a uniform action throughout the embedded tissue, with as little necrosis and as much selective destructive action on the malignant cells as possible. In any case, however, for physical reasons alone, it is not possible to eliminate all necrosis; around each tube inserted there will develop a spherical necrotic area. This necrosis is caused by the intensity of the beta and soft gamma radiations in the immediate neighborhood of the tube. Because the bulk of the soft radiations mentioned have a limited range of penetration around the tube, the necrotic areas surrounding the tube differ very little in size in proportion to the increase of emanation contained in different tubes. Bagg has shown by experiments on animals that within a period of two months there is practically no difference in the size of the necrotic areas (they are all 1 cm. in diameter) caused by tubes containing any quantity of emanation between 0.1 and 5 mc. Tubes of a strength outside of these extremes are almost never used at the Memorial Hospital. Therefore, areas of necrosis 1 cm. in diameter around each tube cannot be avoided. Two provisions, a proper separation of the tubes within the tumor tissue, and the use of tubes containing a proper quantity of emanation, will limit necrosis between the unavoidable necrotic areas around the tubes. These two provisions will cause the destruction of the neoplasm to depend on a selective action on its cells by the cross-firing of the more deeply penetrating beta and gamma radiations, the ideal in radium therapy.

The burying of emanation filtered through 0.4 mm. of platinum in place of unfiltered emanation has been suggested recently by Dr. Regaud of Paris, and is now being thoroughly tested and developed by him and Dr. Cesbron with the hope that this modification will produce the same

good end-results as unfiltered emanation, and with less necrosis and discomfort to the patient.

These directions for dosage may be counted upon to cause complete retrogressions of operable and many inoperable epidermoid carcinomas and many other forms of cancer; and to do so in favorable cases without the risk of operation, and with less discomfort, less subsequent deformity, and less danger of recurrence than by operation. The amount of discomfort involved in this method of treatment varies much with the stage at which the growth is treated. For early favorable growths, even in such sensitive organs as the tongue, the discomfort is not severe—in its worst stage about two or three weeks. Many cases of carcinoma of the cervix go through the whole post-therapeutic course without sensation. Second treatments produce more severe reactions. Heavy dosage in advanced growths should not be attempted; much suffering is endured by patients who are treated for advanced lesions, though it is often difficult to estimate for how much of it the treatment, as opposed to the disease itself, is responsible. On the other hand, many surprises have been encountered: patients making complete or almost complete retrogressions have stated that from the day of treatment their discomfort has continuously diminished.

The emanation introduced within the tissue in the manner described, undergoes a continuous decay at a uniform rate, diminishing to one-half its value in 3.85 days. As a consequence, after the lapse of a certain period, the embedded tubes become inert, and are either encysted or sloughed out, according to the character of the tissue around them. The total dosage administered from a tube containing any quantity of emanation may be expressed by multiplying the contained quantity of emanation by 132; thus, if a tube contains 2 mc. the dose delivered by it may be expressed as 264 mc. hrs. This method of expressing dosage of buried emanation is useful only for comparative purposes. It does not mean that the activity of the tube ceases after 132 hrs., but merely that the total dosage may be compared to that delivered by a tube containing 2 mgm. of radium element for 132 hrs.; but only compared to this dose,

because the radium element for the same length of time undergoes no diminution in quantity, and therefore, its intensity is constant. The emanation, however, becomes continuously less, and in consequence, more especially during the latter period of the delivery of its total number of millicurie hours, falls off progressively in intensity.

The size, shape and structural type of the tumor must be considered in determining the dosage and distribution of the tubes throughout a tumor. The larger the tumor, the greater is the total dosage and the greater the amount of emanation which may be contained in each tube; though both these factors do not increase proportionately with the size of the tumor. Another factor tends to equalize the amount of emanation used in tubes for growths of different sizes. In the treatment of small growths with definite deep infiltration, growths, for example, 1 cm. in diameter, experience has shown that a dose of 5 mc., best divided into three tubes, is necessary. On first thought this amount seems excessive; because with much less emanation in each of the three tubes there would still result a coalescence of the three necrotic zones, and therefore of the whole of the growth manifest on the surface. Smaller amounts of emanation in each tube would, however, incompletely care for the invaded periphery of the growth, a region which the surgeons, in cancer of the tongue, for instance, condemn for ¾ to 1 in., and in which additional necrotic areas are not desired. In these peripheral regions only sufficient gamma radiation to produce destruction of the tumor cells by a selective action is needed. The attempt to secure the same end-result by much less emanation than 5 mc. by using a few more tubes (each one, perhaps, containing only 0.1 mm. of emanation) would only increase, as Bagg has shown, the total necrosis.

On the other hand, in very large growths, tubes containing more than 3 mc. are seldom used, although at times tubes as strong as 5 mc. have been used. Concerning the regulation of dosage to the shape of a tumor, relatively heavier doses per cubic centimeter are required by tumors covering large but superficial areas than by tumors of a spherical shape. This fact is especially illustrated by epithelioma of

mucous membranes, which tumors vary within wide limits in their depth of infiltration in proportion to the surface which they cover. Tumors, for instance, whose palpable induration is 0.5, 1.0 and 1.5 cm. in thickness require the same number of tubes (each tube of the same strength per square centimeter of surface extent) because the intensity of radiation from each buried emanation tube falls off in the shape of a sphere. In consequence surface growths require almost as large doses as spherical tumors having a diameter as long as the greatest length of the surface growth.

III
MALIGNANT TUMORS OF THE INTRAORAL GROUP

DOUGLAS QUICK, M.B. (TOR.)

This group is made up almost entirely of the various types of carcinoma. A few of the lymphomas and lymphogranulomas of the tonsil and upper respiratory passages are also included, where they are primary and tend to remain localized here. Otherwise these cases are included under the general group of lymphosarcomas.

Since in all these groups of carcinoma the treatment of primary lesions and that of cervical metastases are dealt with separately, as two distinct parts or stages of the disease, it seems best to review first the treatment of primary lesions, considering later the cervical metastases as a whole.

Of the various intraoral carcinomas it is generally considered that carcinoma of the lip is the most amenable to treatment, and carcinoma of the tongue the most difficult. These two groups will therefore be dealt with in detail, while the other and intermediate groups will be reviewed more briefly.

The order of this portion of the report will then be as follows:

A. The Primary Lesion in Carcinoma of
   - Lip
   - Tongue
   - Tonsil
   - Esophagus
   - Floor of Mouth
   - Mucosa of Cheek
   - Superior Maxilla
   - Inferior Maxilla

B. Other Primary Malignant Intraoral Lesions
   - Neoplasms of the Larynx

C. The Cervical Metastases
   1. Of Intraoral Carcinoma
   2. Of Other Types of Intraoral Malignant Tumors

CARCINOMA OF THE LIP

There is probably no field in which the possibilities of radium therapy are more important than in epithelioma of the lip. Of all the epidermoid carcinomas it occupies, at once, the most conspicuous and accessible location. It is, comparatively, very frequent in occurrence. Early in its course it causes subjective symptoms and leads the patient to seek advice. Of all forms of cancer it offers least excuse for failure to make a correct early diagnosis. So strongly do we feel about this that I will say frankly we are, in most instances, opposed to a biopsy as an aid to diagnosis. To anyone familiar with epithelioma the appearance is quite characteristic. At the Memorial Hospital no case is referred for treatment without the opinion of the combined attending staff or a number of its members. We therefore feel that the clinical diagnosis is adequately checked up, once it is reviewed by a number of men all well trained in the diagnosis of cancer. While we favor the taking of tissue for examination, as a general rule, we feel that, for various reasons, most cases of lip epithelioma are exceptions. Many cases present themselves at a stage when a biopsy would mean the removal of a very appreciable percentage of the growth—virtually a partial excision. These growths are surrounded, during their early stages, by zones of lymphocytic infiltration. Removal of a section is very likely to interrupt this infiltration and open wide the channels of dissemination. The procedure is distinctly painful for the patient unless an undue amount of manipulation is carried out to render the area insensitive. The removal of a small neoplastic nodule from the surface of the more advanced lesion is, of course, another matter and can do no harm. The question of manipulation is one which, I think, has not received proper consideration. Since this is one of the few lesions which permit of examination at an early stage, we should not handicap our favorable opportunity by permitting several investigators to squeeze and massage it for the purpose of satisfying what frequently appears to be idle curiosity. If the disease is localized to begin with it has little chance of remaining so after the usual examination in the average clinic.

True epithelioma of the lip, that is, the lesion beginning on the vermilion border of the lip, is always epidermoid or squamous-cell epithelioma.

Basal-cell epithelioma may involve the lip, but if so, it is always by extension from the skin surface beyond the mucocutaneous junction: it should not be classified as true epithelioma of the lip. This extension occurs most frequently from the skin of the upper lip and, as is well known, squamous-cell epithelioma primary on the upper lip is relatively rare.

As is true of epidermoid carcinoma elsewhere, that of the lip presents two distinct types, the superficial papillary and the deeply infiltrating ones. These present, in their early stages, marked differences both histologically and clinically. They also show considerable difference from the standpoint of prognosis. The superficial papillary type early in the disease presents an ulcer of varying size frequently covered by a crust which drops off and reforms periodically. If this crust be removed carefully the surface of the ulcer will be found covered by small characteristic neoplastic nodules; the base is but slightly infiltrated, giving the impression of a lesion set upon the lip rather than invading it. The ulcer may be of considerable extent, frequently covering the greater part of the mucosa of the lip or even appearing as isolated islands of ulceration. The chief characteristic is this early extension at the expense of the mucosa with deeper infiltration only in the later stages. This type responds readily to surface radiation. Glandular involvement is rare until the disease has progressed to the point of invasion of the deeper structures of the lip.

The deeply infiltrating type is characterized by a relatively small area of surface ulceration at first. The ulcer is always deep in its infiltration, with raised indurated edges, and may be crateriform in appearance, with central sloughing. The growth progresses by invasion of the deeper structures in a more or less spherical manner, so that on palpation it presents a well-circumscribed globular tumor. In this type the surface ulceration gives no indication of the extent of the disease. It is a much more malignant growth than the superficial papillary type and is often more difficult to influ-

ence by radiation. Extension to the cervical nodes is earlier and more frequent.

Surgical experience with cancer of the lip has been relatively favorable, compared with the results obtained in epidermoid carcinoma elsewhere. Ewing[1] quotes Fricke as placing the cures at 60 per cent and Steiner at 70 per cent for a five-year period. He also notes that surgical experience emphasizes the necessity of a bilateral neck dissection. Ribera y Sans[2] reports 96 operative results, with 2 deaths, and 80 apparently cured, although not all of these have passed even the three-year period. In a series of 200 cases Dollinger[3] reports 158 primary lesions in which operation gave 70.7 per cent free from disease for three years and 69.6 per cent for five years. In a report of 33 cases Bloodgood[4] found 26, or 78.7 per cent, well for five years. In 21 of these cases no metastases were found in the lymph-nodes removed, and of this group 20, or 95 per cent, remained well five years. Of 12 cases showing metastases in the nodes only 6, or 50 per cent, remained well five years. In a series of 516 cases operated upon, Broders[5] was able to trace 306. Of the group traced, 182, or 59.5 per cent, were living and 169 or 92.8 of the living were free from disease. The average duration of the postoperative period was 7.76 years. One hundred and five patients with metastases were operated upon and of these 69 were traced: 12 were living, and of these 10 were free from disease for periods ranging from 3.29 to 11.73 years. No patient with extension to the deeper cervical lymph-nodes, or to more than one group of nodes, was known to be alive. Von Bonsdorff[6] places three-year curves at 80 per cent and has made the further interesting observation that 90 per cent of recurrences occur before the end of the third year. The difficulty of tracing post-therapeutic lip cases, especially, is very great, because many patients cannot be impressed with the seriousness of their condition and disappear from observation immediately the lesion or wound is healed. For this reason statistics are only approximately correct, and it would be by no means fair to classify as unfavorable all patients who failed to report their condition subsequently. However, a fair approximation would seem to place the results at about 70 per cent clinically free of disease for a five-year period.

Such results would be excellent were they not obtained at the expense of great sacrifice of tissue. It is true that the radical surgical procedure, with a seven-out-of-ten chance of winning, is but a slight sacrifice in dealing with a disease which is so often fatal. It is also true that, as long as we offer such a procedure as the final word, the average layman will hesitate to accept it until his best chance is lost. While it is no fault of surgery that he hesitates, it is nevertheless human nature.

The surgical procedure itself is open to criticism on two points. In dealing with the primary growth the usual method is the V-shaped incision. While this is termed a deformity of no consequence, it is nevertheless an uncomfortable deformity in most instances, especially if an adequate operation has been done. The base of this incision is upward whereas the broad spreading infiltrating base of the neoplasm is downward. When we consider the two types of lip epithelioma, it is at once evident that the greater amount of tissue is sacrificed in dealing with the less malignant of the two forms; and it is undoubtedly, in many cases, the hesitancy on the part of the surgeon to make a sufficient sacrifice that accounts for so many local recurrences in the scar. To say the least, the method is both awkward and unscientific.

In dealing with the cervical nodes the routine bilateral block dissection is followed as the orthodox procedure. This surgical viewpoint has been forced by the fact that a much higher death-rate ensues, once metastases have become firmly established in the glands. Bloodgood's report of 20 out of 21 cases, in which no metastases were found in the nodes after removal, remaining well five years, is indeed strong evidence in favor of early block dissection of the neck. Only 50 per cent of his cases with glandular involvement remained well five years. In Broders'[5] statistics of 516 cases operated upon, the regional nodes were removed in 449 cases, or 87 per cent. Of these, glandular metastases were found in only 105, or 23.38 per cent. In other words, 344 patients, or 76.6 per cent—at least nearly that number, allowing for some failures to demonstrate existant metastases—were operated upon unnecessarily. If every case with

cancer of the lip is to be subjected to such a blanket rule, an appalling number of unnecessary operations must be undertaken. The method does seem unscientific.

Would it not be better to attempt to ascertain whether the death-rate would be increased, by separating those cases in which metastases are most likely to occur from those in which they probably will not occur? We know that the superficial papillary type of growth is much less likely to extend to the nodes. We know also that age and rate of growth are factors of consequence.

After classifying the cases in this manner would it not be possible also to ascertain whether the death-rate would be increased by following an expectant plan of treatment and reserving our surgery until a definite node is palpable? It is true that the cooperation of the patient is necessary for the period of observation; but I believe that with proper instruction and adequate follow-up through Social Service work the number of losses or mistakes can be reduced to a negligible percentage. According to Von Bonsdorff's statistics, this would not mean frequent examinations for the remainder of the patient's life.

By intelligent cooperation on the part of the patient it is possible, in the average neck, to palpate the involved node before its capsule is perforated. In this stage the node performs a conservative function. It demonstrates the direction in which the metastasis is progressing through the lymphatic channel, and holds the disease in check until it can be intelligently dealt with. It has been my experience that a dissection at this time usually reveals only one or two nodes involved. It is rare that a chain of nodes is found involved until late in the disease. This seems true of all cervical metastases of intraoral epidermoid carcinoma. The mode of dissemination itself is a factor in favor of conservatism. I believe we are now fairly well agreed that cancer cells do not grow along the lymphatic channels like a vine along the ground, but that extension is by embolism.

If we add to our expectant plan of treatment of the nodes the use of the physical agents as well, it seems to me we are approaching the problem in a much more scientific manner than before.

In our work at the Memorial Hospital we have divided the treatment of epithelioma of the lip into two distinct parts, which will be dealt with later.

Treatment of the Primary Lesion

The primary growth in the lip lends itself admirably to the application of radium, and in the treatment of this part of the disease we feel very strongly that surgery occupies no place. The location is such that surface radiation can be applied from three sides, and for this we employ the method previously described by the late Dr. Janeway.[7] It is to Dr. Janeway that we owe practically all of our present technique in the treatment of this disease.

A mold of the lesion is made of dental modeling compound. This is held in place by the teeth, and care is taken that it fits well down into the buccogingival groove inside and extends well beyond the limits of the lesion externally. This mold is taken to the laboratory, where, with a heated tool or gouge, furrows are made in it into which filtered tubes of radium are placed. These tubes are then sealed in place by pouring melted paraffin over their surface. For filtration we employ tubes of 0.5 mm. silver, which removes approximately 95 per cent of the total radiation. These tubes are sunk into the mold to the depth of 4 mm. in order to give a more equal distribution of radiation, and are so arranged that one tube is available for each square centimeter of surface to be covered. Care is taken that the tubes extend well beyond the palpable borders of the growth. With this method an excellent cross-fire is obtained. The rigid mold conforms accurately to the contour of the lesion, and since it is made to fit between the teeth it must remain exactly in place. For lesions of ordinary size a dosage of 60 to 65 mc. hrs. per sq. cm. of surface is employed; but if very extensive this is slightly reduced because of the curved surface and amount of additional cross-fire. The most important point in applying radium in this manner is to have the tubes extend well beyond the limits of the growth in all directions.

This method of radium application is employed in practically every case of lip cancer. For the primary papillary type of growths and for many of the deeply infiltrating ones

it is all that is necessary. Usually one application is sufficient to effect a complete regression of the growth.

In certain deeply infiltrating recurrent growths, as well as in primary lesions of similar type, it is necessary to supplement this surface application by burying emanation in the substance of the neoplasm. For this purpose small glass capillary tubes 3 mm. in length and 0.3 mm. in diameter containing not more than 1 mc. of radium emanation are inserted interstitially by means of fine trocar needles, and left in situ. The use of 1 per cent novocaine as a local anesthetic renders the procedure painless and simple. Emanation buried in this manner decreases in value at the rate of approximately 15 per cent per day, so that a very prolonged radiation is effected. Since the capillary tube removes little more than the alpha rays, the full intensity of both beta and gamma rays is obtained in the most inaccessible portions of the growth. One mc. of emanation gives a total radiation equivalent to about 132 mc. hrs. We have had no ill effects from the small glass capillary tubes as foreign bodies, but I believe it is always wise to employ surface radiation first, even though an interstitial application is contemplated from the beginning. The external radiation renders much more remote the possibility of dissemination of malignant cells, by the trauma of introducing the needles.

Statistics of Treated Cases

During the past four and a half years we have treated at the Memorial Hospital 162 cases of epithelioma of the lip. A considerable percentage were recurrent cases and many of these were very well advanced. I am convinced that several cases would have been better off had no treatment been given. There comes a period in the course of the disease when we must recognize the fact that it is too late for even the palliative use of physical agents.

In this series of 162 cases, 92 were primary without demonstrable cervical nodes, 11 were primary with nodes, and 59 were recurrent.

Of the recurrent cases 16 were recurrent in the nodes only, 26 at the local site only, and 17 both locally and in the regional nodes.

Of the entire series 115 cases have been traced to date and 47 untraced. We have found it very difficult to trace many of our earlier cases, because once free from evidence of the disease, many patients feel that they are then brought back only to satisfy the curiosity of the physician. More recently we have made it a point to instruct the patient, or a responsible relative, as to the gravity of the condition. This, together with a careful follow-up through our Social Service department, has been productive of encouraging results. While we ordinarily classify all untraced cases as having been victims of the disease, it seems unfair to extend this to all the lip cases. Some of the trouble here is due to indifference on the part of earlier patients.

Of the 115 cases traced, 80, or 69.6 per cent, are now free from disease. Of these, 16 are of over three years' duration and 4 over four years' duration. The average period of freedom from clinical evidence of the disease is eighteen months.

Twenty-seven cases are known to have died and 8 more are steadily becoming worse. In all, 22 neck dissections have been done following the plan previously outlined. Fifteen are now clinically free from disease for periods ranging from four months to four years, the average being eighteen months for the group. Six cases died at periods of four months to two years after operation, the average duration of life following operation being fourteen months. One case has recently recurred and is steadily becoming worse.

Of the 92 cases primary without palpable nodes at the time of admission, 9, or 9.8 per cent, developed nodes subsequently. Of these, 8, or 90.2 per cent are now, following combined radiation and surgical dissection, clinically free from disease for periods of four months to over four years, the average period being nineteen months. One patient died of recurrence nineteen months after the neck operation.

Of this series of 92 cases primary without palpable nodes at the time of admission, 67, or 72.8 per cent, are now known to be clinically free from disease. Two died of the disease and another died of apoplexy, although at that time clinically free from carcinoma. The remaining cases of the series have been untraced.

Conclusions

In our opinion the primary lesion in epithelioma of the lip should be managed entirely by the use of radium. For the average case surface radiation is sufficient, while in a few of the more deeply infiltrating lesions this surface application should be supplemented by the use of radium emanation embedded interstitially.

The cervical nodes should be treated conservatively. External radiation to the neck is indicated at once in all cases admitted for treatment. Following this, cases without palpable nodes should be kept under observation after a sufficient period of external radiation. If nodes are present or appear subsequently, a complete unilateral neck dissection under local anesthesia, coupled with the use of radium emanation in very weak tubes buried throughout the wound, is indicated. Dissection of the opposite side may be done subsequently if indicated by the presence of nodes. External radiation following operation is advisable in the majority of cases.

While the time factor is still too short to permit of comparison with surgical statistics, we feel convinced from our experience in this group of unselected cases that radium deserves the foremost place in the treatment of lip cancer. If properly applied it bids fair to produce results surpassing our present surgical statistics. These results can be obtained with a minimum sacrifice on the part of the patient. Except in the event of a neck dissection, his daily work need not be appreciably interrupted. The resultant scar is, in most instances, scarcely discernible. By the conservative treatment of cervical nodes a vast amount of needless surgery can be eliminated. All this tends to remove doubt and fear from the mind of the patient and promises to bring him for advice and treatment at an earlier and more favorable time in the course of his disease than heretofore.

Bibliography

1. Ewing, J. Neoplastic Diseases. Philadelphia, 1919, p. 816.
2. Ribera y Sans, J. Cancer des Levres. *Soc. Internat. Chir.*, (11th Congress) 1908, i, 26.
3. Dollinger, J. Lippenkrebse. *Soc. Internat. Chir.*, (11th Congress) 1908, i, 37.

4. Bloodgood, J. C. Cancer of the Lower Lip. *Boston M. & S. J.*, 1914, clxx, 49.
5. Broders, A. C. Squamous Cell Epithelioma of the Lip: A Study of 537 Cases. *J. Am. M. Ass.*, 1920, lxxiv, 656.
6. Von Bonsdorff, I. G. Ueber die Behandlung des Lippenkrebses. *Soc. Internat. Chir.*, (11th Congress) 1908, ii, 16.
7. Janeway, H. H. The Treatment of Cancer of the Lip by Radium: A Report of Twenty-four Cases. *J. Am. M. Assn.*, 1918, lxx, No. 15, p. 1051.

CARCINOMA OF THE TONGUE

Carcinoma of the tongue has proven itself to be one of the most difficult types of malignant disease with which to deal. The microscopic anatomy is rather uniform but the clinical course varies extensively. On the whole it may be said that growth is rapid and dissemination early. This is probably due to the rich vascular and lymphatic supply, and to the constant movement of the organ. While it is relatively accessible, it is, nevertheless, much more often fatal than many other more inaccessible types of cancer. It terminates fatally in 75 to 90 per cent of cases, according to Warren, Butlin, and Meller.[1] In frequency, Jessett[1] places it second only to carcinoma of the cervix, while Jacobson[1] gives it third place. The average duration of life in untreated cases is less than two years.

In the treatment of this disease surgery alone has, for various reasons, proven inadequate and unsatisfactory. Many cases come to the surgeon in the inoperable stage, thereby leaving a large group in which surgery offers nothing —in fact, worse than nothing, if an ill-advised operation is attempted. In our own series of cases only 27 per cent were operable at the time of applying for treatment. This figure is, of course, too low, because, especially in our earlier work, we received none but very advanced cases. It is encouraging to note, however, that recently we have been getting much earlier cases for treatment.

The location of the lesion on the tongue has a great deal to do with determining its operability. Bastianelli[2] has noted that those on the tip of the tongue are most favorable for operation, while of those at the base he has not seen a single cure, and advises against operation.

We frequently see the primary lesion operable but the glands inoperable. In a considerable percentage of cases, operable as far as the extent of the disease is concerned, the general condition of the patient is not sufficiently good to withstand the surgical shock. Many of these patients are suitable subjects for pneumonia or some other intercurrent infection following the radical surgical procedure. In view of these considerations, we see at once that surgery occupies a limited field in the treatment of the disease as a whole.

Within the operable field, surgical statistics vary to a considerable extent. Meller[1] found that operation prolonged life 13.4 months, cured 14.6 per cent and had a mortality of 13 per cent. Morestin[3] placed the operative mortality at 20 to 25 per cent, Capetti[4] at 11.6 per cent and Poirier[5] at 25 per cent. In his series of collected cases, Bastianelli[2] found 11.6 per cent well over three years. Butlin,[6] in a review of 197 cases, found 55, or 27.8 per cent, well from three to twenty-three years. Of those dead a much larger percentage was from recurrences in the glands than from recurrence of the local lesion. He had no cases well following operation on recurrences.

In an analysis of 777 cases, Capetti[4] found 18 per cent free from disease over three years, and from a group of selected operators noted that this percentage was raised to 20. Caird,[7] in an analysis of 60 hospital cases, found, at the time of his report, 16 survivors. Of these, 10 cases were well one year, and the others twenty, twenty-four, thirty and thirty-one months and seven and eight years, respectively.

In a report of 30 cases from Boston City Hospital, Lathrop and Scannell[8] had 2 cases alive seven and five years respectively, both from partial excisions. Of those dead, the longest period of life after operation was two years.

Cobb and Simmons[9] of the Massachusetts General Hospital reported 56 cases of carcinoma of the tongue, 34 of which were operated upon. The types of operation ranged from the simplest to the most radical. The immediate operative mortality was 8.5 per cent, and of the 34 cases, four were alive and well at the time of the report, 2 cases thirteen years, 1 case six years and 1 four years. Another

died of some intercurrent disease at the end of four and a half years. Including this last case, their cures were 14.3 per cent. They have noted, also, that all these clinical cures occurred in elderly patients.

In view of these collected surgical statistics it is quite evident that much remains to be hoped for in the treatment of cancer of the tongue.

In our own work we have divided the treatment of this disease into two distinct parts, of which later mention will be made.

Treatment of the Primary Lesion

In the treatment of the primary lesion we feel very strongly that surgery occupies no place, and that this part of the disease belongs entirely to the radium field.

In our earlier work with surface applications of radium we were, on the whole, disappointed; so much so that in our 1915–1916 report Dr. Janeway stated: "By the time carcinoma of the tongue becomes over one centimeter in diameter the possibility of healing it with radium becomes uncertain."

Based on the knowledge at hand at that time, I believe his conclusion was correct as far as the use of radium on the surface is concerned. Only 1 of the 4 cases reported clinically free from disease in that report still remains well.

Shortly after that period we began burying radium emanation in the substance of the growth, and by this change in technique we feel that our results have been immeasurably improved.

While we have not discarded surface applications of radium in tongue cancer, we feel that its use in this way is confined to the treatment of certain very superficial growths, such as some of those beginning in leucoplacic areas, to the cases of basal-cell carcinoma which we very rarely meet with in the tongue and to supplementing doses of buried emanation. The bulk of our treatment rests entirely upon the use of buried emanation. For this purpose we use fine glass capillary tubes about 3 mm. in length and 0.3 mm. in diameter, each containing about 1 mc. of radium emanation. I specify 1 mc., or slightly less, as being the most satisfactory

strength to use at present. In our earlier work we used tubes of 2, 3 and 4 mc., but found that they produced too much necrosis of tissue.

Radium emanation decays at the rate of about 15 per cent per day so that the total value of 1 mc. is equivalent to approximately 132 mc. hrs. of continuous radiation.

These weak tubes are buried uniformly throughout the growth by means of fine trocar needles, and left in situ. In order to make this as painless as possible the lingual nerve is injected with 1 per cent novocaine, or, if the lesion be far back on the tongue, infiltration with novocaine is used. The dose of radium applied in this way depends, of course, upon the size of the lesion, although the average is probably from 6 to 15 mc. The shape of the lesion also has something to do with the amount necessary, since it is quite evident that a bulky, spherical lesion requires relatively less than one of the elongated type extending for a considerable distance along the lateral border of the tongue.

Uniformity of distribution and accuracy of approximation throughout the growth are the all-important factors, and, in case the fixed number of tubes determined upon is insufficient to fill these requirements, it is advisable to use more tubes of weaker individual values.

While the use of radium emanation in this manner is, in many respects, comparable to burying steel or gold needles containing radium element, still there are certain features of difference. By the use of emanation tubes a more intense beta-ray effect is obtained throughout the entire area, since the emanation is filtered only by the thin wall of the capillary tube which removes only the alpha rays. A very prolonged radiation of both beta and gamma rays obtained by this method is, we feel, superior to the shorter exposure of mainly gamma rays made necessary where metal containers with large amounts of the element are inserted in the growth and removed after a few hours.

The tissue reactions incident to this very prolonged radiation over a period of weeks are very important. The amount of trauma is less and distribution can be made much more uniform and accurate by burying the emanation tubes. The emanation decreases in value at the rate of approximately

15 per cent per day, so that in about four days one-half of its energy has been spent, while at the end of eight days approximately one-fourth of its activity is still present. It will thus be seen that radiation is carried out over a prolonged period without the discomfort to the patient of having foreign bodies, subject to being dislodged, projecting into the oral cavity. By this means the dosage can be very materially increased. In this particular connection I would warn those using needles containing the salt, that they should not attempt to equal the dose for emanation in carrying out a parallel technique with their metal needles.

By this method of treatment the radium reaction is both prolonged and intense, and is by no means painless, so that during its course every encouragement must be given the patient lest he feel that he is becoming worse rather than better. Scrupulous care must be directed toward cleansing the mouth. Nourishment must not be decreased, and the patient's general physical condition must be kept at as high a level as possible.

Statistics of Treated Cases

During the past three and one-half years we have treated at the Memorial Hospital 148 cases of cancer of the tongue. A large percentage of these were very far advanced and some of them, I believe, would have been better had no treatment been given. We cannot escape the fact that there comes a period when it is too late for even the palliative use of physical agents.

In this seires of cases, 134 or 90.5 per cent were in men and 14 or 9.5 per cent in women. This, I believe, is rather a low proportion of females. Piquantin[1] found from an analysis of collected cases that 17 per cent of cancer of the tongue appeared in women. A history of syphilis was obtainable, either in the direct clinical history, or by a positive Wassermann reaction, in 35.1 per cent of all cases. This would probably have been higher had a Wassermann reaction been done in every case. Nearly all of the men were excessive smokers, 84.5 per cent of all cases giving a history of its use. Bad and irregular teeth were very common throughout. All the women had a very definite history of dental irritation,

excepting one, and this one had a positive Wassermann reaction and leucoplacia of the tongue.

The average duration of the disease in this series was 6.72 months, the rather high average being due probably to a few long-standing cases of one to seven years.

Of the series, 69 cases, or 45.8 per cent, were primary growths without glands, and of these only 34, or 23 per cent of the total, were classed as surgically operable. Of this number (34 cases), 29, or 85.3 per cent are now clinically free from disease for periods of two months to over three years from the time of beginning treatment. One died, a year after treatment was begun, with recurrences both locally and in the glands. One left our service eleven months after treatment was first given, was operated upon elsewhere, and when last heard from was still free from disease. One patient was lost track of after six months. One died of diabetes one and a half years after treatment, with no clinical evidence of carcinoma present, and the fifth died eighteen months after his first treatment, from extension to the neck, which he refused to have treated as we had advised.

Of these 34 primary operable cases without glands, 5 subsequently developed cervical metastases. All were treated by the combination of surgery and radium, and 3 are now clinically free from disease. As stated above, one died a year after treatment with both local and cervical metastases, and the other was lost track of at the end of six months. Of this same group 30, or 88.2 per cent, were verified by microscopic sections.

Of the primary cases coming to us with glands at the time of admission, only 3 cases, or 2 per cent of the total, were operable at this time. These were treated as previously outlined and all are now clinically free from disease.

The total number of primary cases coming to us with and without glands at the time of admission was 128, or 86.5 per cent of the total series. In a large number of these cases, the extent of either the primary lesion or the cervical nodes rendered the case surgically inoperable.

Of the recurrent cases applying for treatment there were 20, or 13.5 per cent. Six of these had recurred locally only. Four recurred in the glands only, while 10 were recurrent

both locally and in the glands. Three of these cases were surgically operable. They were all local recurrences and were treated locally by burying radium emanation. Two are now clinically free from disease for periods of two and one-quarter and one and three-quarters years respectively, while the third has been lost track of.

Of the total series, 40 cases, or 27 per cent, were operable at the time of admission, and of this group there are at present 34 cases, or 85 per cent, clinically free from disease for periods, as previously mentioned, ranging from two months to three and one-half years.

Of the total series, positive biopsies were obtained in 133 cases, or 89.8 per cent.

As to the method of treating these primary lesions, most of it has been by the burying of radium emanation tubes. One hundred and twenty-eight cases were treated by this method alone. In 5 cases surface applications of emanation filtered by 0.5 mm. of silver and held in place by an applicator made of dental modeling compound was the only method of treatment. In 9 cases a combination of buried emanation and surface applications was used. Two primary lesions were too advanced for any form of treatment and 4 recurrent cases involved the glands only.

External radiation to the neck, with heavily filtered radium, has been used in 24 cases, or 16.2 per cent. In those cases developing cervical nodes after treatment of the local lesion, the average time between the primary treatment and the gland appearance has been a little over four months, the extreme ranges being six weeks to twelve months.

Of the entire series, neck dissections, as will be subsequently outlined, combined with the use of radium in the wound, have been done in 58 cases, or 39 per cent. Of these there has since been recurrence in 15 cases, or 25.8 per cent of the operated series.

There are to date in our total series 43 cases, or 29 per cent, clinically free from disease for periods ranging from three months to over three years, as follows:

6 cases clinically free from disease 3 to 6 mo.
7 cases clinically free from disease 6 to 12 mo.
13 cases clinically free from disease 12 to 18 mo.

6 cases clinically free from disease 18 mo. to 2 yrs.
7 cases clinically free from disease 2 to 2½ yrs.
4 cases clinically free from disease 2½ to 3½ yrs.

In addition there are 18 cases where radium caused a complete retrogression of the primary lesion but in whom there were hopeless neck recurrences.

Adding these, therefore, to the previous group of cases clinically free from disease, we have 61 cases, or 41 per cent of all the local lesions showing complete retrogression. There are 19 cases, or 12.8 per cent, still improving but not as yet free from disease. Fifty-eight cases, or 39 per cent, are dead, although three of them were clinically free from carcinoma at the time of their death. One case died of diabetes, another of pneumonia, and a third of cardiorenal disease. Twenty-one cases, or 14.1 per cent, have been lost track of, so that we must add them to the unfavorable group. Seven are still living, but are gradually becoming worse. Twenty-one cases, or 14.1 per cent of the entire series, were, in my opinion, unimproved by treatment. These were cases with very advanced disease, in most instances extremely advanced both locally and in the regional glands. I believe they would have been better off for the remaining short period of life left them, had no radium been used. Many advanced cases, however, were benefited for a time.

Of the group of cases clinically free from disease at the present time, the average age is fifty-seven and seven-tenths years, the extreme ranges being thirty-two to seventy-eight years.

Conclusions

In our opinion the primary lesion in cancer of the tongue should be managed entirely by the use of radium. The use of buried emanation in weak tubes uniformly distributed throughout the growth is by far the method of choice in applying the radium. The cervical glands should be treated conservatively: first by external radiation where the neck is free from palpable involvement. Should metastases then appear, the treatment of these should be external radiation,

followed by a conservative neck dissection under local anesthesia, coupled with the use of radium emanation in very weak tubes buried throughout the wound.

While the time factor is still too short to permit of comparison with surgical statistics, we feel convinced that the form of treatment in unselected cases will yield a much higher percentage of clinical cures than will surgery alone in the selected operable group.

Bibliography

1. Ewing, J. Neoplastic Diseases. Philadelphia, 1919, p. 818.
2. Bastianelli, M. R. *Soc. Internat. Chir.* (11th Congress, Rome) 1908, i, 80.
3. Morestin, H. La Cure Radicale du Cancer de la Langue. *J. de Chir.*, 1919, xv, 221.
4. Capetti, L. Traitment Chirugical du Cancer de la Langue. Thesé, Paris, 1907.
5. Poirier, P. Curabilité du Cancer en Général et du Cancer de la Langue en Particulier. *Bull. Acad. de méd.*, Par., 1906, lxx, No. 36.
6. Butlin, H. T. The results of operations for carcinoma of the tongue with an analysis of 197 cases. *Brit. M. J.*, 1909, i, 1.
7. Caird, F. M. Epithelioma of the tongue: A review of 60 hospital cases. *Edinb. M. J.*, 1911, vi, 5.
8. Lathrop, H. A. and Scannell, D. D. Results of treatment of cancer in and about the mouth at Boston City Hospital. *Boston M. & S. J.*, 1905, clii, 421.
9. Cobb, Farrar and Simmons. Results in Cases of Carcinoma of Tonsils, Tongue and Jaws Operated on at the Massachusetts General Hospital, January 1, 1892 to January 1, 1900.

MALIGNANT TUMORS OF THE TONSILS

A review of the literature on new growths of the tonsil emphasizes several surprising features. Malignant tumors in this location are considered rare, and, with a few exceptions, reports are of individual cases. The question of diagnosis is uncertain in many reports. The opinion seems to prevail that carcinoma occupies a minor place in the entire group, while a loose classification of sarcoma covers the majority of cases. In spite of its accessibility and early symptomatology the older methods of treatment have accomplished probably less here than in any of the intraoral group.

In view of this fact it seems advisable to report on the results obtained to date with radium.

Because of the difficulty in deglutition, neoplasms of the tonsil are usually noted early, but unfortunately they rarely receive proper attention at this stage. Valuable time is usually lost in using local caustic applications followed by antisyphilitic treatment, and when these fail it is a common thing to find an incomplete tonsillectomy performed. The liberties taken with tonsillar ulcers seem out of proportion even to those taken with other intraoral new growths. It frequently happens that a correct diagnosis is not made until the disease recurs locally or appears in the cervical nodes. The factor of error seems greatest in carcinoma of the tonsil. This is probably due to the fact that the ulcer is small and slow-growing and that palpation, as a means of clinical examination, is seldom resorted to. This type of growth, however, predominates in older subjects, especially after the third decade. In young patients lymphosarcoma is the most common neoplasm encountered. It assumes various atypical forms and hence we find in the literature many varieties of sarcoma reported in the tonsil. In fact, all of these probably belong to the group of lymphosarcomas or malignant granulomas.

The report and extensive résumé made on this subject a few years ago by Matthews[1] is most instructive. He considers practically all cases surgically inoperable and points out that, even in cases apparently localized, the prompt recurrence following surgical removal indicates that infiltration at the base is more widespread than is apparent. This is especially true of lymphosarcoma. Matthews concludes that, with the methods in practice at the time of his report, the cure of malignant disease of the tonsil was effected in only a small percentage of cases and that the operative procedures which promised most chance of cure were so extensive as to be attended with considerable mortality. This referred especially to lateral or external pharyngotomy. Of the more limited procedures he felt that tonsillectomy was of little value, but that tonsillectomy plus cauterization gave a much better chance. With tonsillectomy alone, in 20 cases of sarcoma and 3 of carcinoma, presumably early and favorable cases, not one was reported to have lived two years without recurrence, and only 3, all sarcomas, were reported without

recurrence at periods of between six months and one year. He felt that in children, especially, radical treatment was of little avail and usually detrimental. Of cases treated by tonsillectomy and cautery he found 15 reported cases with 1 free from recurrence after three years. In this group Jacobson's[2] case is the longest reported without recurrence—eleven years. Of Matthews' own 22 cases, only a few of which came to operation, there were no cures. In his group of collected cases there were 84 of sarcoma. Of these, 11 remained without recurrence six months to one year, 5, one to two years, 6, two to three years and 1, over three years. The case going over three years was the one treated by combined tonsillectomy and cautery. Of those between two and three years, 1 was the result of combined tonsillectomy and cautery, 4, lateral pharyngotomy, and 1, Coley's toxin without operation. In the collected group of 23 carcinomas he found 1 case without recurrence six months to one year, 3 cases one to two years and 3 over three years. Two of the cases over three years were by combined tonsillectomy and cautery.

Of the other operative procedures practically no good results were reported. The method of exposure by cheek splitting gave no case over two years without recurrence. This method was probably not resorted to, however, except in very advanced cases. Dawbarn's method of ligating both external carotids and injecting paraffin into the vessel on the affected side gave no results worth mentioning. In Jacobson's report the cures by open-mouth methods is placed at 10 per cent. This rate is, however, questionable because the time interval was short and the group of cases small. Matthews noted the palliative relief afforded by *x*-ray in some cases. Decrease in pain and retardation of growth were the benefits observed from this agent.

Various other observers have noted the palliative effects of *x*-ray, but all reports are of one or very few cases, and no reported complete regression is of sufficient duration to make it of statistical value.

A few isolated reports are also to be found on the use of radium, either alone or in conjunction with *x*-ray. In these the time interval is short, and the final results inconclusive except in so far as they relate to palliative relief. In a number

of them the radium dosage was hopelessly small. A very recent report of a case by Perrier[3] is most interesting. He reports an extensive lymphosarcoma treated by the Janeway[4] method of burying radium emanation in tubes, both in the tonsil and cervical nodes, and clinically free from disease at the time of his report—two months after the close of treatment.

This method of treating new growths of the tonsil with radium emanation buried interstitially was first introduced in our work over five years ago by the late Dr. H. H. Janeway, and has proven of inestimable value.

It has been our experience that, in comparison with other intraoral neoplasms, those of the tonsil are particularly susceptible to radium. This may be due to the fact that in young subjects the active lymphoid tissue exerts a strong defensive force, while in later life the lack of blood supply and resultant tonsillar atrophy favors the action of radium. Once the disease has extended beyond the tonsil, however, the problem becomes more complex. The same cancer tissue seems to be influenced in its degree of malignancy by the nature of the soil in which it grows.

As the disease advances in the tonsil, one very common extension is that across the base of the anterior tonsillar pillar to the tongue. In this location it is quite as difficult to deal with as a primary carcinoma of the tongue. We feel that, in cases where this involvement is present when the patient is admitted to the service, the prognosis is only about 50 per cent as good as it would be were the disease confined entirely to the tonsil. Extension to the other adjacent structures—anterior tonsillar pillar, soft palate or lateral pharyngeal wall—is equally as complicating except in so far as the relative accessibility is concerned. In the tongue, infiltration is deeper and more ill-defined. This is due to greater thickness of tissue, a rich blood supply and the free motion of that organ.

Treatment of the Primary Growth

We feel very strongly that all malignant tumors primary in the tonsil, unless very far advanced, should be treated by radium entirely. Furthermore, a clinical classification, based on the ultimate result to be hoped for, should

be made at the beginning of treatment. In other words, a distinction should be made between the case with possibilities for complete regression of the disease and the other, for which palliation only can be expected. Treatment should be given accordingly.

Some of the very far advanced cases should resort to medicinal measures rather than the physical agents for temporary relief.

Thorough and efficient radiation of a new growth of the tonsil designed to cause a complete regression of disease necessitates putting the patient through a very painful period. Unless this complete regression can be reasonably expected, such a procedure is unwarranted. Hence the need for classification before beginning treatment. While the tonsil is readily exposed to vision, it is not so readily accessible to the older methods of radium application. Previous to 1916, when we were using only surface radiation, we would do no more than give palliative relief. It is impractical to make an accurate and satisfactory surface application of radium to the tonsil for a period of time long enough to afford proper dosage. Even with radium tubes held in place by a hook at one end we were unable to maintain the accuracy and intimacy of application necessary for uniform results. However, as soon as we began the use of radium emanation buried interstitially, our results at once improved. In carcinoma, 1 mc. of radium emanation per c.c. of tumor tissue is approximately the required dosage. With lymphosarcoma or malignant granuloma, on the other hand, only about one-half this amount is usually required. It is always best to aim at complete regression from a single dose. It entails less suffering on the part of the patient, and furthermore, a subsequent dose can never be as accurately placed because of the surrounding inflammatory tissue. The amount of fibrosis following the first massive dose renders a second dose less effective and is also more apt to be followed by hemorrhage from a rapid breaking down of this fibrous tissue. Wherever subsequent treatment is necessitated following an initial massive dose, the patient should be kept under close observation until all slough has separated; or the external carotid artery should be ligated as a precaution.

Where treatment is to be given for palliative purposes only, much smaller amounts should be used, and these can be supplemented from time to time without at any period exciting an extremely painful reaction. In treating these advanced cases, care should always be taken to prevent making them worse. The tendency is of becoming too optimistic over faint possibilities of controlling the disease entirely, and thus pushing treatment too radically.

In introducing the emanation tubes with trocar needles care should be taken to make the distribution as accurate as possible, with the greater concentration of dosage toward the base of the neoplasm rather than near its surface. Two points are of special importance in locating the tubes. One of these is at the base of the anterior tonsillar pillar, to block off extension to the tongue. The other is the lowermost part of the lesion, frequently just out of sight unless the indirect method is used. Failure to place the emanation properly at this point may permit extension of the disease to the lateral pharyngeal wall or the extreme base of the tongue before it is recognized. In order to introduce the tubes more accurately here we use curved trocar needles and introduce them by the indirect method.

In cases of recurrent new growths of the tonsil, which, unfortunately, we see only too frequently, the problem of radium introduction is difficult. The anatomy is very much altered and recurrence or implantation is usually at the periphery. In these cases the emanation tubes must be placed very widely.

The question of trauma must always be considered in using emanation tubes interstitially. Wherever possible, a surface application of filtered radium should be used a few days before introducing the tubes. In the tonsil this can be done very efficiently by placing heavily filtered radium over the tonsillar area, externally. Our own plan is to use 2000 to 2200 mc. hrs. filtered by 2 mm. of brass and placed 3 cm. from the skin surface just posterior to the angle of the mandible. We feel that this renders emboli due to trauma much less harmful, thereby relieving in large measure the danger of introducing the trocar needle.

Statistics of Treated Cases

During the past five years we have treated 149 cases of malignant neoplasms of the tonsil.

Many of these were very advanced cases, frequently recurrent after operation; and as we review the work three errors must be recognized, especially in the early part of the series. A large group of cases were so advanced that I am convinced they would have been better off had no radium been used. There comes a time in the course of the disease when medicinal measures give more relief than the physical agents. Some cases which should have been classified for palliative treatment only were treated too vigorously in the hope of obtaining a complete regression of disease. In these the treatment defeated its own purpose. In our earlier work with buried emanation the tubes used were for the most part too strong, so that an unnecessary amount of suffering was produced to obtain a result which can now be attained with more comfort and less danger.

Our present follow-up of these cases shows the following results: Of 124 cases of carcinoma of the tonsil, 28 are now clinically free from disease. Two other cases were free from clinical evidence of disease for fifteen months, at which time they were lost track of. Twenty cases at present under treatment are progressing favorably and a fair number, at least, bear promise of a complete clinical regression of the disease.

Forty-one cases were definitely improved for varying periods of time, but finally either died of the disease or are steadily becoming worse. Improvement in these cases means slowing up or definite regression of the growth, relief from pain, reduction in size of cervical nodes or prevention of their breaking down and fungating externally. Twenty-seven cases were absolutely unimproved by treatment and 10 more were completely lost track of, so that they must be classified with those totally unimproved. Of the carcinomas, 10 were recurrent cases, 2 of which were with recurrent cervical nodes and an unrecognized primary lesion in the tonsil. Twenty-four cases belonged to the group of lymphosarcomas or malignant granulomas. It is my impression that a few more cases belonging in this group are filed under the

general heading of lymphosarcomas, and hence were inaccessible for this report. Of this group 6 cases are now free from clinical evidence of disease. One shows an excellent palliative result of over three years' duration, but at no time has he been entirely free from clinical evidence of the disease. Six of these cases were recurrent.

One case of rhinoscleroma of the tonsil is of interest. The patient has been under treatment for over three years, the growth at times showing an apparent complete regression, only to reappear at some adjacent area of mucosa.

Of the 28 cases of carcinoma of the tonsil reported clinically free from disease at present, the average duration since the initial treatment is twenty-six months. The longest period is fifty-six months and the most recent four months. In 10 cases neck operations were performed, and in these the average duration is twenty-eight months. The oldest is fifty-six months and the most recent six months.

Another case of interest from a palliative standpoint was admitted eighteen months ago, with an advanced primary growth and metastases in both sides of the neck. This patient has been treated by burying emanation, entirely, and while he has not a complete regression there is nevertheless complete temporary control and no subjective symptoms. This case is cited simply as an example of palliative relief.

Of the lymphosarcomas, or closely allied lesions, 1 case has had a complete regression for over four years, another, sixteen months, 1, twelve months, 1, eight months and 2, six months each. Another case was lost track of a year and a half after treatment, with complete regression at that time. One of the most interesting cases in this group is a patient in whom the tonsillar lesion cleared up promptly, but a large mass appeared in the neck and another in the lower left quadrant of the abdomen. Under heavy radiation these were reduced somewhat and have remained stationary and quiescent without treatment for two years. His initial treatment was over three years ago.

Conclusions

In general, lymphosarcoma, because of its extremely cellular structure, responds very promptly to radium, and the

area treated tends for the most part to remain well; but dissemination is early and widespread, and it is doubtful if many permanent results can be hoped for from radiation of the local process.

Bibliography

1. Matthews, J. Malignant tumors of the tonsil. *Laryngoscope*, 1912, xxii, 737.
2. Jacobson, N. Malignant disease of the tonsils. *Ann. Surg.*, 1901, xxxiii, 280.
3. Perrier, C. Lymphosarcoma of the tonsil treated with radium. *Rev. méd. de la Suisse Rom.*, Oct. 1921, xli, 10.
4. Janeway, H. H. Treatment of cancer, particularly of the tongue, tonsil and rectum, by buried emanation. *Am. J. Roentgenol.*, Feb., 1920, vii, 92.
   Radium Therapy in Cancer at the Memorial Hospital. Hoeber, New York, 1917.
5. Goris. Pharyngectomie pour Lymphosarcome de l'Amygdale. *J. de chir., Brux.*, 1911, xi, 12.
6. Watson, W. P. Case of lymphosarcoma of the tonsil and palate. *Bristol M. Chir. J.*, 1920, xxxvii, 51.
7. Goodale, J. G. Lymphosarcoma of the tonsil. *Boston M. and S. J.*, 1908, clix, 409.
8. McCoy, John. Surgical treatment of cancer of the tonsil with a report of cases. *Laryngoscope*, 1919, xxix, 422.
9. Canuyt, G. Epithelioma de l'Amygdale Gauche. *Rev. de larygol.* [etc.], *Par.*, 1918, xxxix, 12.
10. Freudenthal, W. A case of sarcoma of the tonsils treated with radium: cure. *Internat. J. Surg.*, 1908, xxi, 12.
11. Harris, T. J. Neoplasm of the tonsil, probably malignant, treated by the *x*-ray with apparent benefit. *Laryngoscope*, 1906, xvi, 220.
12. Edling, L. Sur un Cas de Sarcome de l'Amygdale traite par les rayons X et par le radium. *Cong. Internat. de physiothér., C.-r.*, 1911, 685.
13. Anschutz. Demonstration Eines mit Radium bestrahlten Tonsil Carcinoms. *Verbandl. d. Ver. deutsch. Laryngol.*, 1914, xxi, 332.
14. Bertolotte, M. Sopra un caso di Carcinoma della Tonsille guarito colla Rontgen-radium-therapie. *Radiol. med.*, 1915, ii, 155.
15. Quick, Douglas. The conservative treatment of cervical lymphatics in intraoral carcinoma. *J. Am. M. Assn.*, Aug. 6, 1921, lxxvii, 436.
    Treatment of carcinoma of the tongue. *Ann. Surg.*, June, 1921.

CARCINOMA OF THE ESOPHAGUS

Our experience in this field has been very disappointing. At first thought one might feel that new growths in this location should be favorable for treatment by radium because of accessibility through the esophagoscope, and because of

the supposed early symptomatology. Unfortunately, our experience has not borne this out.

The esophagus is a very thin walled tube, and by the time the patient begins to take the first symptom—dysphagia—seriously, the disease has involved the entire wall or has gone beyond it. We have repeatedly seen an apparent complete healing as viewed by the esophagoscope, only to find a definite extra-esophageal mass demonstrable by roentgenogram. If the lesion be localized to a portion of the circumference of the organ, it is difficult to protect the normal mucosa opposite the growth from the damaging effects of radium. Dosage which we know will adequately care for epidermoid carcinoma elsewhere produces such a reaction (inflammation followed by fibrosis and constriction) that it is impractical. The danger of an acute mediastinitis following severe radium inflammation must not be forgotten, and damage to other vital mediastinal structures must also be considered.

In view of this we have been forced to modify our massive doses, as far as the esophagus is concerned. We have found that smaller doses, more frequently repeated, tend to control the disease with less shock to the patient. With less local inflammatory reaction the stricture is kept open, rather than hastened in its constriction. This decrease in plan of dosage is at first sight not in keeping with our general plan of radium treatment. However, we have more recently attempted to overcome the bad effects of large intra-esophageal dosage by a division or shifting of radiation. As previously mentioned, the internal dose is cut down and repeated more frequently. This is supplemented by heavy external radiation, with either radium or *x*-rays, directed from all four sides of the chest. This plan has given better palliative results with less discomfort to the patient.

Our present plan is to introduce within the stricture a string of ½ mm. platinum tubes of radium emanation arranged end to end in rubber tubing and of sufficient number to go well beyond the limits of the disease above and below. A dosage of 200 mc. hrs. per tube is well tolerated by the patient and can be repeated within a few weeks. These tubes should always be introduced through the esophagoscope. A bulb of adhesive plaster on either end of the string of

tubes holds it well in place within the stricture, and a long linen thread attached to the upper end serves to withdraw it. If, as occasionally happens, the tubes cannot be introduced in this manner, the patient is given a heavy linen cord to swallow, a gastrostomy is done and the tubes drawn up into the stricture at the time of this operation. External radiation has been by *x*-ray or radium "pack" from all four sides of the chest and repeated as frequently as the skin and the patient's general condition will permit.

We have not insisted on a gastrostomy in every case, but I am of the opinion that it should be done. It is a simple operation which can readily be performed under local anesthesia. It puts the esophagus at rest and relieves the growth from irritation, and it provides at once for adequate feeding. Too often the gastrostomy is done as an emergency affair when the patient is too weak to regain strength through this aid of last resort.

Within the period covered by this report we have treated 92 cases of carcinoma of the esophagus. We have not a single case that we can class as clinically cured. The best result was in a patient who had a complete healing of the esophageal ulceration and apparent relief of all symptoms for a prolonged period. He died fifty-one months after his first treatment in another hospital and no autopsy was obtained. For the last few months of his life, his general strength waned and vague chest symptoms indicated a periesophageal extension of the disease.

A considerable number of these cases were in my opinion ill-chosen for treatment by radium. The disease was far advanced and I believe a gastrostomy would have given more relief than either radiation or radiation plus gastrostomy.

Many of the patients were improved for a period of a number of months, the stricture was kept open, and the rate of growth of disease slowed up. This is more especially true of the later cases where a smaller internal dose and intensive external radiation were used.

While the series is very discouraging as a whole, we feel that our experience, especially with these later cases, encourages us in following the plan of gastrostomy, moderate, repeated internal radiation and intensive external radia-

tion, with the hope of giving, at least, a much longer period of palliative relief.

CARCINOMA OF THE FLOOR OF THE MOUTH

Practically all malignant lesions in this location are epidermoid carcinoma, and treatment varies but little from the plan already outlined. The anatomical factors and relation to surrounding structures are the chief points to be mentioned in treatment here. The arrangement of muscular planes is such that the disease infiltrates widely and early. One of the striking features at autopsy has been the extension far backward beneath and into the base of the tongue.

It is only in very early cases that the tongue is found uninvolved: the tendency is to invade the tongue from below upward.

The body of the lower jaw limits extension of the disease externally, but from pressure the periosteum is readily involved, so that secondary invasion of the bone is rather common.

The main part of the treatment of these growths is by buried emanation.

This can to advantage be supplemented by external radiation from various angles, depending on the location of the lesion. If it be in the anterior portion of the floor of the mouth, a dental compound applicator filled with ½ mm. silver tubes can be applied to the surface. This should be done a few days before the bare tubes of unfiltered emanation are introduced, in order to minimize the danger of dissemination of disease by trauma. If the growth be at one side or the other, heavily filtered radium applied at a distance from the skin surface through the submaxillary zone is advantageous, and if the growth be in front, through the submental area.

The danger of hemorrhage is no greater than in other intraoral lesions and should be dealt with on the merits of the individual case.

If the neck is exposed surgically either for ligation of the external carotid, lingual facial vessels, or for removal of glands, advantage of this exposure should be taken to introduce bare tubes into the extreme base of the growth from below.

Large doses of radium buried close to the jaw are apt to damage the bone to such an extent as to devitalize a portion of it. This cannot, however, be avoided where the disease is in intimate contact with the jaw. The period of sequestration is prolonged. With separation of this shell of bone, healing takes place rapidly.

Within the period of this report we have treated 60 cases of carcinomas primary in the floor of the mouth. The majority of these were advanced cases. Only an occasional one could be classed as surgically operable, and few as favorable, from a radium standpoint.

Of the 60 cases, 18 were primary without palpable cervical nodes. Six were recurrent cases, 2 locally only, and 4 both locally and in the cervical nodes. The remaining 36 cases were primary with definite involvement of cervical nodes. In carcinoma of the floor of the mouth extension to the cervical nodes is early and widespread in the sense that nodes on both sides of the neck are apt to become involved at an early date.

Of the total group, 16 cases are now free from clinical evidence of disease for periods of eight to forty-eight months, the average for the group being twenty months. Eighteen cases were definitely improved for a period of several months. Seven cases are still improving and it is hoped that some at least will later show complete regression of the disease.

The remaining 19 cases were either unimproved or were lost track of, and must be classed with the unimproved.

CARCINOMA OF THE MUCOSA OF THE CHEEK

It might seem that epidermoid carcinoma in this location would be relatively favorable from the standpoint of treatment. Unfortunately, such is not the case. Invasion of the masseter and adjacent muscles occurs early, so that definition of the extent of the disease is difficult. Frequent movement of these muscles tends toward dissemination of the disease. Infiltration of the muscle quickly causes trismus, so that proper exposure for treatment is exceedingly difficult. Extension to the cervical nodes occurs early and in a considerable percentage of cases.

Altogether, carcinoma in this location has been one of the most difficult to deal with of any of the intraoral group. In our experience the degree of malignancy has been greater than with practically any other group. Treatment has been chiefly by buried emanation. Even in lesions that appear early and localized we feel that a generous amount of interstitial radiation is necessary to control the disease.

If the lesion is located well forward the buried emanation may be supplemented by a dental compound applicator filled with ½ mm. silver-filtered radium applied to the internal ulcerating surface. In all cases, heavily filtered radium should be applied externally over the base of the growth. For this we employ 2000 to 2200 mc. hrs. filtered by 2 mm. of brass applied over the cheek at a distance of 3 cm. from the skin.

In many of the cases the disease had extended on to the soft parts over the upper or lower jaws. This had to be dealt with as a primary jaw growth with the proximity of bone as the complicating factor.

Within the period covered by this report we have treated 44 cases of carcinoma primary in the mucosa of the cheek.

Of this group 24 were primary without definite palpable involvement of the cervical nodes. Eleven were primary with involvement of nodes. The remaining 9 cases were recurrent: 3 were local recurrences, 2 were recurrent in the cervical nodes only, and 4 both locally and in the nodes.

Of the total group, 11 cases have now been free from clinical evidence of the disease for periods ranging from four to forty-eight months, the average being twenty-seven months. Seventeen cases were definitely improved for periods of several months, and 5 cases are still improving, although the final outcome is uncertain. The remaining 11 cases were either unimproved or untraced.

CARCINOMA OF THE INFERIOR MAXILLA

In this location the most difficult problem is the close apposition of new growth to bone, or, as so frequently seen, actual invasion of bone by the neoplasm. This introduces a very difficult problem, in that efficient radiation frequently results in destruction of a portion of bone, which, after a

prolonged period, separates as a sequestrum. If the jaw is extensively invaded by carcinoma it is probably best to remove it surgically after very heavy radiation. Trismus is another trying complication if the growth is located far back along the alveolus.

The majority of these cases have bad teeth, and these act as irritants, frequently keeping the mouth very foul until they are removed. The removal of all such teeth is imperative.

Radium application in carcinoma of the lower jaw is by buried emanation, supplemented by dental modeling compound applicators filled with ½ mm. silver-filtered radium, if the growth is accessible to such. External radiation by heavily filtered radium is not resorted to as much as in new growths of the mucosa of the cheek or tonsil.

In this group we have to report at the present time 69 cases. Of these, 25 were primary without palpable cervical nodes, although most were very advanced locally. Twenty-eight were primary with definite involvement of cervical nodes; 16 were recurrent, 2 of these recurring locally only, while 14 were recurrent both locally and in the cervical nodes.

Of the total group, 13 cases are now clinically free from disease for periods ranging from ten to forty-eight months, the average being twenty-four months. Twenty-six cases were improved for several months, and 14 more are still improving. The remaining 16 were either unimproved or lost track of.

CARCINOMA OF THE SUPERIOR MAXILLA

Malignant lesions coming under this heading may be subdivided into two groups: those beginning in the mucosa over the alveolar ridge and those beginning in the superior maxillary antrum.

Those of the former group are subject to the same general remarks and form of treatment as growths of the inferior maxilla. Late in the course of the disease they tend to perforate the antrum by destroying the bone forming its floor.

Those arising in the antrum present a different picture both clinically and in the method of treatment best adapted

to them. Carcinoma in this location tends to be a localized disease for a considerable period. Frequently the first clinical evidence of it is an indurated, non-ulcerating swelling over the prominence of the cheek, an elevation or exophthalmos of the eye, or a fungating growth projecting downward inside the cheek alongside the alveolus. In any event, these signs indicate a perforation of the bony wall of the antrum by the new growth. All growths within the antrum must be properly exposed before efficient treatment can be administered. Unless the gross extent of the disease or the general physical condition of the patient contraindicates it, our plan has been to remove that portion of the alveolus forming the floor of the antrum. This permits of free exposure and free drainage. The growth may then be removed with a curette and radium placed in the central part of the cavity, or unfiltered radium emanation may be buried throughout the mass of tumor tissue. In addition, heavily filtered radium is applied over the antrum externally. For this our plan has been 2000 to 2200 mc. hrs. filtered by 2 mm. of brass and distance of 3 cm. from the skin surface. The results in this group have been most encouraging.

In the group arising in the mucosa over the alveolar ridge we have 44 cases. Of these 24 were primary without nodes, although very advanced locally in nearly every instance. Ten cases were primary with cervical nodes involved, and 10 were recurrent. Of the recurrent cases 1 recurred locally only, while 9 recurred both locally and in the cervical nodes. Of the total group 9 cases now show complete clinical regression of disease over periods of nine to forty-two months, the average being twenty-five months. Seventeen cases were improved for a number of months and 5 are still improving, although with the final outcome doubtful. The remaining 13 cases were either unimproved or lost track of.

In the group arising within the antrum we have 36 cases. Of these, 20 were primary without cervical nodes palpably involved, but in most instances with involvement of the bone. Seven cases were primary with nodes and 9 were recurrent. Two cases were recurrent locally only, while 7 were recurrent both locally and in the cervical nodes. Of the total group, 8 cases are now clinically free from disease for periods

ranging from six to thirty-nine months, the average being twenty-seven months. Fourteen cases were improved for a time, and 5 are still improving. The remaining 9 were either unimproved or lost track of.

MISCELLANEOUS—INTRAORAL

Because of their location and relation to cervical node involvement several smaller groups should be mentioned at this stage of the report.

New growths of the soft palate, unless very advanced, respond well to the use of radium. Treatment is best managed by means of very weak bare tubes of radium emanation buried within the growth, since surface applications are very difficult and practically impossible. Weak tubes are preferable because of the danger of destruction of tissue. Of 9 such cases treated, 6 are now free from clinical evidence of disease for periods ranging from four to thirty-two months, the average being fifteen months.

New growths primary in the mucosa over the hard palate are more accessible to treatment than those of the soft palate and can be managed best by a combination of buried emanation and surface-filtered radium. The chief danger is from invasion of the bone by disease and destruction of bone by radiation. Of 12 cases treated, 7 are now free from clinical evidence of disease for periods of four to forty-two months, the average being sixteen months.

An interesting feature of these cases is the large percentage of adenoid cystic epitheliomas of salivary-gland type found in this location.

Six cases of carcinoma apparently primary in the mucosa of the lateral pharyngeal wall all did badly. In this location the disease is usually well advanced before a diagnosis is made. Infiltration is widespread and ill-defined. The location and uncertainty of extent of disease render treatment difficult, while intensive radiation seriously interferes with deglutition.

Another interesting group is the carcinomas beginning in the Schneiderian membrane of the nose. These produce a rather characteristic clinical picture, but unfortunately are,

as a rule, well advanced before recognized. Treatment is best managed by a combination of unfiltered emanation buried interstitially and filtered radium applied in rubber tubing through the nose as well as externally at a distance from the skin, as previously described. Of 21 cases treated we now have 6 clinically free from disease for periods of nine to twenty months, the average being sixteen months.

Occurring in the nasopharynx and posterior portion of the nasal passages we find a varied group of new growths. Epitheliomas arising from mucosa at almost any point, especially over the turbinates and about the entrance to the Eustachian tube, fibrosarcomas, especially in young subjects, arising from the posterior extremities of the turbinates, and lymphosarcomas from the lymphoid tissue in the vault of the nasopharynx have been met with in our experience. Unfortunately, our system of filing under general headings of the disease does not permit of an accurate statistical report of these cases.

NEOPLASMS OF THE LARYNX

This has been a most interesting group. While we have had a rather large series of cases, they have been almost invariably extremely advanced in the course of the disease. We feel, however, that from them we have gained considerable valuable experience in the use of radium in the larynx.

A proper classification of these cases at the time of admission to the service is imperative. This may be done in various ways. From the surgical standpoint they may be classed as operable or inoperable. In the former group, we recognize the value of surgery or a combination of radium and surgery. With us this group has been very small, but we have been inclined to use radium entirely and our experience to date has confirmed us in this decision. In the inoperable group radium offers a great deal. For those cases on the borderline of operability there is hope for a complete regression of disease. In the more advanced cases it gives relief by slowing up the disease, decreasing its bulk, lessening discharge and pain and reducing the danger of hemorrhage. Finally there is the group of very advanced cases for whom the physical agents are contraindicated.

From the anatomical standpoint, classification may be on the basis of intrinsic or extrinsic origin. This is important because of the fact that greater liberty may be taken with radium dosage in the extrinsic cases.

From a purely radium standpoint classification should be on the basis of whether complete regression of disease can be reasonably anticipated or whether treatment is for palliative purposes only. In the former cases, we feel that we are justified in putting the patient through a severe radium inflammatory reaction in order to obtain the desired result. This is not the case with those for whom only palliative relief can be expected. Here the patient's comfort throughout must be the governing factor.

Accuracy and intimacy of radium application is the all-important factor in laryngeal work. Dosage should always be massive or maximum. Our best results have invariably been obtained by this method. Fractional doses tend to fibrosis, and consequently to protection of the malignant cells. It is true that there are certain dangers attendant upon such dosage, such as surface burns, sloughing and acute edema. There is, however, no danger as great as that of the disease itself.

All cases accepted for treatment, whether favorable or unfavorable, promising for complete regression or only palliative, should be treated by external radiation. For this our plan has been 2000 mc. hrs. filtered by 2 mm. of brass, applied at a distance of 3 cm. from the skin on either side of the larynx. This affords an excellent cross-fire of radiation which very definitely inhibits the growth. We have not seen complete regression of epidermoid carcinoma follow its use alone. Subsequent doses of external radiation must depend on the course of the individual case.

For extrinsic laryngeal growths the internal radiation is best accomplished by burying radium emanation tubes of not over 1 mc. each throughout the growth, allowing approximately 1 tube per c.c. of malignant tissue.

For the intrinsic lesions no blanket rule obtains. In some cases with plenty of air space, weak emanation tubes in small dosage may be employed safely and to advantage. In others a single ½ mm. platinum tube in rubber, or two tubes arranged in tandem may be introduced into the cocainized larynx and

held in place by a stiff wire until a dosage of 200 mc. hrs. per tube has been given.

The question of tracheotomy as a necessity or as an aid to efficient treatment must be decided on the merits of the individual case.

For some localized growths, especially papillomas, we have found the following to be most efficient: a very strong bulb of unfiltered radium placed on the end of a pliable rod so that it can be applied directly against the growth and held in place by the indirect method for a short time.

In some of the rare cases of lymphosarcoma or granuloma of the larynx, external radiation alone is sufficient to cause a complete regression of disease.

We have treated in all 91 cases of new growths of the larynx. Of these 81 were carcinomas, 7 papillomas and 3 lymphosarcomas or malignant granulomas.

Of the carcinomas, 8 cases are now free from clinical evidence of disease for periods ranging from eight to forty-two months, the average being twenty-one months. One other case died from pneumonia after a period of thirty months' freedom from evidence of disease. A large group of cases were improved for a time, but ultimately succumbed or are gradually becoming worse. A number are still improving. In reviewing the work I am convinced that a considerable number of very advanced cases would have been better off had no treatment been given.

Of the papillomas, 4 cases are now free from clinical evidence of disease for periods of twelve to forty-two months, the average being twenty-six months. One patient left the service at the height of his radium reaction and was operated upon elsewhere, and 2 have been untraced.

By the use of unfiltered radium applied over the surface of these localized nodules we feel that our results are now very much improved.

The 3 cases of lymphoma have all shown complete regression of disease for periods of six, twelve and fifteen months respectively. Two of these cases were treated by external radiation only, as previously described, while the third received a combination of external radiation and filtered radium internally.

TREATMENT OF CERVICAL LYMPHATICS IN INTRAORAL CARCINOMA

It has long been recognized that the successful treatment of intraoral cancer depends more upon the treatment of the cervical nodes than of the primary lesion. During the past twenty-five years radical changes in the surgical treatment of cervical nodes have taken place.

In 1895, Butlin[1] began a complete dissection of the anterior triangle on the affected side as a routine procedure in every case of intraoral carcinoma. This was followed and amplified by others. Within a few years the procedure was extended, as a routine, by many operators to both anterior triangles. The work of Crile[2] in this country, setting forth the principle of removing en bloc all lymphatic tissues of the neck, has remained the standard about which various modifications have been made.

The work of Sir George Lenthal Cheatle,[1] in which he demonstrated the invasion by malignant cells of the deeper lingual muscles in tongue cancer, brought the suggestion of a wider excision of the primary growth. This was coupled with the block dissection idea and soon a complete removal of the primary lesion and lymphatic structures in one piece was advocated. Morestin[3] favored this, but confined his neck dissection for the most part to the side of the neck on which the lesion was situated. He did, however, advise a removal of all structures that could be sacrificed adjacent to the lymphatic chains of the anterior triangle. Butlin was in favor of Cheatle's plan for wide excision plus block dissection in the more advanced cases, but he admitted that his own statistics did not bear out this opinion. He also advocated the doing of the neck dissection before the appearance of definitely involved nodes and stated that his results were improved thereby. In his report, however, he cited 8 cases operated upon after nodes had appeared, with 3 successes; and 70 cases operated upon before nodes appeared with 24 successes. This does not indicate a benefit from doing an early dissection. Many operators did a two-stage operation, removing first the primary lesion and second the gland-bearing area, to avoid infection and the higher mortality incident

to a single operation. Crile[2] favored this method. Others insisted on a complete removal in one stage. Warren[4] was very emphatic on this point because of his belief in extension of the disease by direct permeation of lymphatic channels. In a recent excellent analysis of the cervical lymphatics, with particular reference to carcinoma of the tongue, Jamieson and Dobson[5] have pointed out the multiple channels of dissemination. Based on this they consider the block dissection of Crile inadequate in dealing with most tongue lesions. In this particular type of intraoral carcinoma their plan may be briefly summarized as follows: Early lesions of the lateral border of the tongue require a complete unilateral block dissection with intrabuccal excision of the primary growth. In more advanced lesions in any of these locations and in all lesions of the back of the tongue they advise bilateral block dissection with extrabuccal excision of the primary lesion. They noted that this latter operation is impossible at one sitting, highly dangerous at two and only to be done with any degree of safety at three sittings; also that it is difficult to induce patients to submit to a three-stage operation. Their technique of block dissection entails briefly a complete removal of the sternomastoid muscle, internal and external jugular veins, a considerable area of deep fascia of the neck and all the groups of lymphatic glands—lower and upper deep cervical, submaxillary and submental. In the bilateral operation the internal jugular vein is left on one side.

Such then is, very briefly, the trend of surgical experience in dealing with the cervical metastases of this group of carcinomas. What have been the results?

The very fact that the principle of more radical neck surgery has met with almost universal approval in surgical circles is proof enough of its superiority over the older methods. Definite comparative statistics on this point by the same operator are scarce. Andrews[6] quotes Crile as stating that the older methods gave 29 per cent of cases well after three years while his new technique gave 52 per cent well after three years. The present surgical position has been forced by the fact that the death-rate from intraoral cancer was increased once the disease became firmly established in the cervical nodes. In an effort to circumvent this, then, the only thought has been to

remove as many glands as possible as early as in the course of the disease as possible.

There are other considerations, however, which we must bear in mind. All patients suffering from intraoral cancer, even though the lesion may be early, are not physically able to withstand such an operation. In some groups of cases the operative mortality is comparatively low, while in others it is higher. In following his radical technique with tongue cancer, Morestin[3] had an operative mortality of 20 to 25 per cent. In another analysis of tongue work Meller[1] found that the radical procedure prolonged life 13.4 months, cured 14.6 per cent and had an operative mortality of 13 per cent. Apart from the operative mortality we must consider the subsequent course of the failures from radical operation—very often their condition is rendered worse rather than better. It is true that the ordeal of such a radical procedure is but a small sacrifice if it gives a fair hope of recovery; but as long as we are forced to offer it to the public as the only hope for a gambling chance the average layman will avoid it until his best chance is lost.

It would be very interesting and instructive to know what percentage of glands removed in the routine block dissection are actually invaded by malignant cells. Many observers have assumed that nearly all are, but no one has demonstrated it. Practically all reports on the results of radical neck dissections fail to state the percentage of glands found involved by microscopic examination.

Bloodgood[7] has contributed strong evidence in favor of an early block dissection. Of 21 lip cases showing no demonstrable involvement of nodes at the time of their removal, 20 remained well for five years. Of his cases with glandular involvement, only 50 per cent were still well at the end of this period. In a series of 516 lip cases reported by Broders,[8] neck dissections were done in 449, or 87 per cent and metastases found in 105, or 23.38 per cent. In other words, 344 patients, or 76.6 per cent—at least nearly that number, allowing for some failures to demonstrate existant metastases—were operated upon unnecessarily. Lip cancer is undoubtedly the most favorable of the intraoral group for surgical treatment, and the average results show about 70

per cent well five years after the complete operation. The tongue, on the other hand, is probably the most difficult to deal with. In a series of 802 cases collected by Bastianelli,[9] 584 were followed, and of these 11.6 per cent were free from recurrence after three years. He did not find a single case of cancer of the base of the tongue well after three years even though a radical bilateral operation on the neck had been done.

It would seem, therefore, that if a blanket rule for block dissection of the neck is to be applied to every case that can stand it or will permit it, an appalling number of unnecessary operations must be undertaken, many of them offering at that but a poor chance for the patient.

Would it not be better to attempt to ascertain whether the death-rate would be increased by separating those cases in which metastases are most liable to occur from those in which they probably will not occur? Epidermoid carcinoma presents two distinct types—the superficial papillary and the deeply infiltrating. The former is much less liable to extend to the nodes until very late in the course of the disease. The disease in different locations varies in its capacity for early involvement of the nodes. Carcinoma of the tongue and tonsil extends to the regional nodes much earlier than that of the mucosa of the cheek or lip. While the age of the patient is not an infallible guide, it is nevertheless a strong predisposing factor. The hygiene of the buccal cavity itself is undoubtedly of more importance than is generally recognized. With the oral cavity kept under best hygienic conditions it has been our experience that extension to the cervical nodes is relatively less frequent than where no attention is given to proper cleansing. Ewing[10] has pointed out that changes in the lymph-nodes draining malignant tumors show that the implantation of metastases is preceded by a period of preparation of the soil; the nodes show evidence of septic and toxic absorption for a considerable period.

After classifying our cases in this manner, would it not be possible to ascertain, in a large percentage of the cases at least, whether the death-rate would be increased by following an expectant plan of treatment and reserving our surgery until a definite node is palpable? By intelligent cooperation

on the part of the patient it is possible to palpate an involved node in the average neck before its capsule has been perforated. In this stage the node performs a conservative function and represents one of nature's strongest barriers to dissemination of disease. Ewing[10] has noted that embolic cancer cells may be destroyed in the nodes under some circumstances, but that for the most part the nodes appear to retain and retard growth rather than destroy these cells. Evidence of retardation of growth in the nodes by fibrosis and encapsulation are common. In this early stage of palpable involvement the node demonstrates the direction taken by the metastasis through the lymphatic channel and holds the disease in check until it can be intelligently dealt with. It has been my experience that a dissection at this time reveals usually only one or two nodes involved. It is rare that a chain of nodes is found involved throughout until late in the disease. This appears to be true of all cervical metastases of intraoral carcinoma. It is one of the chief clinical differences between the metastasizing properties of epidermoid carcinoma and the glandular types of carcinoma, such as that of the breast.

The mode of dissemination itself is a factor in favor of conservatism. I believe we are now fairly well agreed that cancer cells metastasize by embolism and not by direct extension along the walls of the lymphatics. Ewing[10] favors this theory and suggests that Handley's idea may be due to the lodging of cell emboli within the lymphatic channels and growth in either direction from these. Jamieson and Dobson[5] believe that extension within the tongue is by permeation of lymphatics, but that extension to the nodes is by embolism. Ryall[11] states that the situation of the primary lesion does not indicate either the chain of nodes or the side on which metastatic involvement may appear. In Broders' large series of lip cases, not a single one with involvement of more than one group of lymphatics recovered.

It would seem therefore that the adoption of a radical block dissection, as a blanket rule, is a frantic rather than a scientific effort borne out by the natural history of the disease, toward preventing its extension.

To add to our argument in favor of the conservative treatment of the nodes from a surgical standpoint, we have now the aid of the physical agents.

During the past few years rapid progress has been made in the use of *x*-rays and radium from the therapeutic standpoint. We have therefore felt disposed to take advantage of these agents and use them in conjunction with surgery where this combination seems justifiable.

In our work at the Memorial Hospital we have used radium almost exclusively in our neck work, although recently we have been doing more external radiation, and for this purpose we are utilizing *x*-rays to a greater extent than previously. During the past year we have endeavored to radiate all necks externally as soon as possible after admission to the service. For the more favorable cases we have used radium, for the remainder, *x*-rays, and in some, a combination of the two agents.

In those cases having no palpable nodes this has been done for the purpose of stimulating the protective defenses in the lymphatics and destroying minute metastatic foci at a time when they are of least proportions. Radiation tends to block lymphatic channels through its effect on the endothelial cells, and on the gland itself the effect is to produce a marked cellular reaction. There is an exudation of the lymphocytes and plasma cells, production of connective tissue is stimulated, and this tends to incarcerate vagrant cancer cells. Thus the natural barriers to cancer dissemination are strengthened rather than removed. We do not feel, however, that with external radiation alone we have ever been able completely to destroy fully developed epidermoid carcinoma in the cervical nodes.

In cases where nodes are already palpable, external radiation, by reason of the effects previously mentioned, inhibits the progress of the disease and renders it, at least temporarily, less malignant, and therefore a safer operative risk. A considerable series of nodes studied microscopically suggests that this result has been accomplished.

In all cases with operable nodes on admission, or developing nodes following treatment of the primary lesion with radium, a neck dissection is undertaken, following external

radiation, as soon as the maximum of inflammatory reaction from treatment of the primary growth has subsided. We feel that as a general rule all such dissections should be unilateral and complete. Cancer, however, is a disease in which each case must be considered individually, and consequently various modifications of the operation must be made. These cannot usually be determined until the deeper structures of the neck are exposed.

In all cases, radium emanation is embedded in the operative field following removal of the lymphatic structures. For this purpose small fine glass capillary tubes 0.3 × 3 mm. in size are prepared, containing 0.5 to 1 mc. of radium emanation. These are embedded at all suspicious points in the wound, especially where the lymphatic channels are severed. Since radium emanation decreases in value at the rate of approximately 15 per cent per day, it will be seen that a certain amount necessary for the dosage decided upon can be buried in the wound and left in situ. We have never had trouble from the minute glass tubes: they readily become incarcerated in a small connective tissue capsule produced by the inflammatory effects of the radiation. One mc. of radium emanation affords a total radiation equivalent to approximately 132 mc. hrs. from the time of its introduction until it is entirely exhausted. Since this requires several weeks, it will be seen that a very prolonged and continuous radiation is made possible, and the fact that the active radiation extends over weeks permits of heavier dosage. The inflammatory effects of radiation are not apparent for several days and therefore have no detrimental effect on the healing of the wound. By burying the emanation directly in the wound a uniform distribution is obtained and radiation may be concentrated on suspicious points. Usually a dosage of 5 to 15 mc. is distributed throughout the operative field, concentrated for the most part at the points of severance of lymphatic channels. This gives a total radiation of from 600 to 2000 mc. hrs. of unfiltered rays. We feel that the utilization of beta as well as gamma rays by this method is a very distinct advantage because of the intense local effect of the beta radiation. We feel also that use of the radium in this manner is distinctly superior to the use of filtered radium

encased in rubber tubes and placed in the wound as a drainage tube might be placed. This method fails to concentrate the radiation at points where it is most needed.

. The use of external radiation following operation is advantageous in some cases, especially over the opposite side of the neck. However, where intense radiation has been used within the wound it does not seem that much is to be gained by further external radiation. It is quite possible to devitalize the tissues by overdoing the use of the physical agents.

As for the operation itself, our procedure has been as follows: Local anesthesia of 1 per cent novocaine, using a combination of the infiltration method for the skin incision and conduction for the deeper structures, is employed. A preliminary hypodermic of $\frac{1}{6}$ to $\frac{1}{4}$ gr. of morphin is advantageous in some cases, but by no means necessary in all. A skin incision is made from over the base of the styloid process and 1.5 cm. posterior to the angle of the jaw downward over the anterior border of the sternomastoid muscle to the episternal notch. This incision is bisected by a second beginning at the tip of the chin. The skin and superficial muscle is laid well back. The next step depends upon the individual case. If the sternomastoid muscle can be satisfactorily retracted it is left in place, otherwise it is divided below and turned upward with the fat tissue and lymphatic structures. The posterior belly of the mylohyoid muscle can usually be satisfactorily retracted. The internal jugular vein is not removed unless a node seems firmly attached to it. Under such circumstances no hesitation is felt in removing it. The upper cervical chain of lymphatics is separated as close to the parotid as possible and if necessary, a portion of that gland is also removed. The submaxillary gland is removed with its surrounding lymphatic plexus and the adjacent submental nodes. Only in cases where a definitely involved node lies suspiciously near to muscles is a portion of the muscle fascia excised. In all cases where the primary lesion remains ulcerated at the time of operation the external carotid artery is ligated and, further to cut off anastomotic circulation, the branches supplying the region of the primary growth are also ligated separately. As Küster[12] has pointed

out, ligation of the external carotid as a routine procedure is perfectly safe. I should like to note, however, that ligation should always be done above the superior thyroid branch to avoid nutritional disturbances through interference with thyroid function. After insertion of the radium emanation tubes, as previously outlined, the wound is closed in the usual manner and drainage provided for the first twenty-four hours, postoperative.

In certain cases we feel that various modifications of this routine method may be made to advantage. In many elderly patients with primary lesion healed or well under control, the dissection may be confined to the submaxillary and submental groups through a submaxillary incision or to the upper and lower deep cervical groups through a sternomastoid incision. In either case, radium is used as before and the procedure in no way interferes with a subsequent dissection of the other group in the event of that becoming necessary.

In all cases where the disease has perforated the gland capsule and is infiltrating widely we feel that it is unwise to attempt a radical surgical removal. Radium emanation in sufficient dosage is distributed uniformly throughout the mass and at other strategic points, and the wound closed. The mass affords an excellent means of retaining the radium in place and thus permits of very heavy radiation of all surrounding parts. In this instance surgery is employed for exposure and accurate localization only. We now have a small group of cases in which all palpable evidence of the disease has disappeared following treatment in this manner. It is the only way in which we have been able to destroy completely well-established epidermoid carcinoma in the cervical nodes.

I should like to emphasize the importance of doing neck surgery under local anesthesia. The patient's head is under complete control; surgical shock is reduced to a minimum; hemorrhage is well controlled; the danger of post-anesthetic pneumonia is avoided; careful work can be done; and many patients can be successfully cared for who could not stand a general anesthetic.

The time factor in this plan of treatment is still short, and our statistics are therefore of little value from a compara-

tive standpoint. We do feel, however, that they are reasonably suggestive. Since the two extremes of intraoral carcinoma may be represented by tongue and lip cancer, our statistics for these may be briefly cited.

Our series of carcinoma of the tongue, reported in December, 1920, for a period of three and a half years previous, comprised a total of 148 cases. Sixty-nine were primary cases without palpable involvement of the nodes, and of these, 34 were classed as surgically operable. Of this group of 34 cases, 29 were free from clinical evidence of disease for periods ranging from three months to three years; 5 cases developed nodes after treatment of the primary lesion with radium. Of these, 3 were clinically free from disease following the combination of surgery and radium. One died a year after operation with recurrences both local and regional, and the other was lost track of.

Of the primary cases with definite involvement of the nodes upon admission only 3 were operable. These were treated with radium for the primary growth and a combination of surgery and radium for the neck. All three were clinically free from disease—the longest case being of nearly three years' duration. Of the recurrent cases, 3 were operable, all were local recurrences, and of these, 2 were well for periods of one and one-fourth and one and three-fourths years without development of nodes to that time, while the third case was untraced.

Of the total series, neck dissections, following the plan described, were done in 58 cases. Of these, recurrences appeared in 15 or 25.8 per cent.

In cases developing nodes after treatment of the primary growth with radium the average period between this treatment and the appearance of the node was four months: the extremes being six weeks and twelve months.

To the time factor of this group of cases another six months may now be added, since all the patients reported clinically free from disease at that time have remained so, with the exception of one in which a recurrence has followed the neck operation. A second operation has recently been done in this case.

Our series of lip carcinomas for the past four and a half years comprises 162 cases. Ninety-two were primary without

demonstrable involvement of the nodes; 11 were primary with nodes; and 59 were recurrent. Of this total group 115 cases have been traced to date. Eighty, or 69.6 per cent, are clinically free from disease for periods ranging from four months to four years, the average period being eighteen months.

Of the 92 cases without nodes on admission, only 8 are known to have developed nodes after treatment of the primary growth with radium, although it is to be supposed that certain others are present in the group of untraced cases. Of these 8 cases, 7 are now clinically free from disease following our usual neck technique, for periods ranging from four months to four years. The other case died of recurrence in the neck one year after his original operation.

In all, 22 neck dissections were done following the plan previously outlined. Fifteen are now free from disease for periods ranging from four months to four years, the average being eighteen months. Six cases died at periods of four months to two years after operation, the average duration of life after operation being fourteen months. One case has recently recurred and is steadily becoming worse.

Conclusions

In making deductions on such a subject as this, the factors presumed, as based on our clinical experience with the combination of surgery and radium, must not be considered proven as yet. The time limit is still brief and methods have changed considerably through this period of four years. We do feel, however, that the results to date are suggestive and very encouraging and that these results warrant us in continuing our effort along the same lines.

Our present opinion therefore may be briefly summarized as follows:

1. The routine block-dissection of the neck in practically all cases of intraoral carcinoma as generally accepted at the present time is a frantic effort without regard for sacrifices, and does not recognize either the natural history of the disease or the various factors which may modify it in individual cases.

2. The cervical lymphatics perform a conservative function in the early course of the disease, and to remove them by

a routine early block dissection removes nature's chief barrier to dissemination, frequently at a time when it is needed most.

3. An expectant plan of treatment which recognizes the natural history of the disease and the natural factors of resistance to it, is an approach toward a more scientific solution of the problem and in no way jeopardizes the best interests of the individual case.

4. The physical agents have demonstrated their worth as a valuable factor in the treatment of this disease and should be used in every case not hopelessly advanced.

5. A combination of surgery and radium offers more than surgery alone, once the indication for operative intervention has arisen.

6. The use of local anesthesia is preferable in all surgery of the cervical lymphatics.

7. A conservative plan of treatment gives promise of reducing practically to a minimum the present immediate operative mortality; of saving patients an appalling number of unnecessary operations; and of saving considerable added suffering following many of these operations. This will react to relieve considerably the factors of fear and distrust on the part of the laity and bring patients into proper channels earlier in the course of their disease.

TREATMENT OF CERVICAL METASTASES FROM INTRAORAL NEOPLASMS OTHER THAN CARCINOMA

These are practically all lymphosarcoma or closely allied diseases. Mention is made of them here only for the purpose of warning against the use of surgery in their treatment. These growths are very cellular and respond promptly to the use of radium, while following surgery the tendency is to rapid local recurrence. The chief danger from these growths lies in their rapid and widespread dissemination to distant organs.

Bibliography

1. Butlin, H. T. Results of operations for carcinoma of the tongue. *Brit. M. J.*, Jan. 2, 1909.

2. Crile, G. W. Cancer of the Tongue. Anoci-Association, Philadelphia, 1914. p. 187.

3. Morestin, H. La Cure Radicale de Cancer de la Langue. *J. de Chir., Par.*, 1919, xv, 221.
4. Warren, J. C. Cancer of the mouth and tongue. *Cong. de la Soc. internat. chir.*, Rap., Brux, 1908, ii, 17.
5. Jamieson, J. K. and Dobson, J. F. The lymphatics of the tongue: with particular reference to the removal of lymphatic glands in cancer of the tongue. *Brit. J. Surg.*, Bristol, 1920, viii, No. 29, p. 80.
6. Andrews, E. W. Keen's Surgery, 1914, iii, 330.
7. Bloodgood, J. C. Cancer of the lower lip. *Boston M. & S. J.*, 1914, clxx, 49.
8. Broders, A. C. Squamous-cell epithelioma of the lip: a study of 537 cases, *J. Am. M. Assn.*, 1920, lxxiv, 656.
9. Bastianelli, M. R. Discussion—de la Resection du Maxillaire inferieur dans les Cancers de la Bouche. Vallas (Lyon) *Cong. de la Soc. internat. de Chir.* (11 Congress) 1908, i, 80.
10. Ewing, J. Neoplastic Diseases. Philadelphia, 1919, pp. 824 and 76.
11. Ryall, C. Cancer of the tongue. *Brit. M. J.*, April 5, 1913, 697.
12. Küster. Treatment of carcinoma of the tongue and ligature of the external carotid artery. *Arch. f. klin. Chir.*, (Langenbeck), 1906, lxxxi.

IV

CARCINOMA OF THE RECTUM

Douglas Quick, m.b. (Tor.)

In reviewing our work of the past few years in rectal cancer it would be quite useless, for various reasons, to attempt a statistical report. Most of the cases treated have been very advanced in the course of the disease, and, while valuable information has been obtained from the radium standpoint, the most that could be hoped for from the patients' side was a certain degree of palliation. The lapse of time necessary for statistics to become of real value has not been great enough. Furthermore, changes in technique have been steadily taking place, so that our earlier work represents in no way what we feel we can accomplish at the present time. This is especially true of the past year.

We are stimulated by the surgical results to date to look for another method of treating rectal cancer and our experience with radium encourages us in proceeding along the present lines.

It is true that during the past few years surgical technique has improved and the operative results are consequently better. In spite of this, in the hands of the most experienced operators the results are poor, and the operation a very mutilating one. More important, however, is the fact that a large number of patients are inoperable when seen by the surgeon. Statistics are not voluminous on this point, but it would seem that, in the opinion of the most radical operators, over 30 per cent are inoperable when first seen. Rennington[1] quotes from the experience of Tuttle and Lynch over a period of nineteen years, that 153 out of 491 cases were inoperable. It is deplorable that so many cases are looked upon as hemorrhoids until the disease is far advanced. Lynch[2] found this to be true in 10 per cent of his series, while Rennington[1] quotes Jones as estimating it at 75 per cent. In

our own experience it would seem that this error was made in well over 50 per cent of all cases. I believe there is no excuse for such errors if the patients' symptoms are considered seriously and a proper examination made.

From an analysis of surgical statistics it appears that the average operative mortality in the best hands ranges from 16 to 20 per cent. Lynch[2] reported 16 per cent in a series of 491 cases. In a series of collected statistics embracing 1665 cases, Hartmann[3] found the operative deaths to be 15.8 per cent and from another series Rennington[1] reports 12.5 per cent to 17.5 per cent, with improvement in the later years. Hartwell[4] reported 26 per cent in 1905 and Mayo[5] 15.5 per cent in 1912. From a series of 1244 cases by fourteen selected operators Lusk[6] reported a rate of 19.7 per cent. Sepsis accounts for a great deal of this immediate mortality and fortunately it has improved in later years. In his report in 1905, Hartwell[4] placed it at 60–70 per cent, and in 1918 Rennington[1] quoted a rate of 39.8 per cent.

In the surgical literature we find considerable use made of the term "cure" as based on a three-year period of observation. I think it would be much better to refer to the result as apparent freedom from disease or "clinical cure" for a fixed period.

Based upon this three-year period of observation, Mayo[5] had 33 per cent of operated cases well for 3 years, and 28 per cent over a five-year period. Rennington[1] reported 218 out of a collected series of 966 cases well three years—about 22 per cent. Hartwell[4] reported 15–20 per cent for this period and Gant[7] 16 per cent "permanent recoveries." In his collected series, Lusk[6] found 16.7 per cent well for the three-year period. Lusk[6] also quoted Baisch as authority for the statement that from a collected series of cases where careful microscopic examinations had been made, one-third of the cases that were otherwise operable showed involvement present in the glands.

A fair résumé of these statistics would then give us the following results: At least 30 per cent of cases are inoperable when first seen by the surgeon. Of the operable group the immediate mortality is at best about 16 per cent. The cases found clinically free from disease at the end of three years

average below 20 per cent, although a few selected groups are reported over 30 per cent.

Granting, therefore, a generous margin of doubt in favor of the surgical procedure, we find that in the best hands an average of 14 per cent of all cases coming to the surgeon are free from disease at the end of three years, and we know, of course, that this rate is lowered with each succeeding year.

This procedure leaves out entirely 30 per cent of the cases to begin with—or gives only a colostomy for relief where it is indicated. It brings to an abrupt end about 16 per cent of the operable cases. In the light of Lusk's report on gland involvement a radical procedure is begun in one out of three cases that it is useless to attempt to complete. It seems unquestionable that many of the cases are rendered more uncomfortable for their remaining period of life, when we consider the physical and mental shock of such radical procedure, the suffering from sepsis in many, and in many others the discomfort of a rectal stoma which does not function comfortably.

Since nearly all malignant lesions of the rectum are either adenocarcinomas or epidermoid carcinomas, we have a certain amount of knowledge of their response to radium from experience with the same types of growths in other parts of the body. The problem is therefore largely one of technique. Unfortunately this is not as simple as it might seem.

In attempting to adapt our technique to the individual case we must have in mind something of what we may reasonably expect to accomplish. A review of our work to date may aid in formulating some such plan.

We have treated in all 161 cases of rectal cancer at the Memorial Hospital during the past four years. Of these, practically all were very advanced cases—many hopelessly disseminated, others advanced recurrences. About 40 per cent of the group represent eleventh-hour efforts to try a new remedy; and as I look back over them I feel sure they would have been better off had no treatment with radium been given. There comes a time in the course of malignant disease when even the physical agents are of no avail.

A large number of cases have been benefited from one to three years and then died of distant involvement or some

intercurrent disease; others are still improving, and some with a fair hope of complete regression of the disease, provided there is not already distant metastasis. By improvement I mean inhibition of the growth, very frequently decrease in its size, with fibrosis which tends to create a local process rather than an actively growing disseminating one. The decrease in size relieves the partial obstruction—constipation is therefore less marked. Bleeding is largely stopped, discharge of mucous is lessened and pain is very materially decreased. With a certain amount of surface healing and deeper fibrosis the amount of septic absorption is lessened. This results in a gain in weight and strength and a general feeling of well-being otherwise not experienced by the patient. In a few cases the palliative relief has been prolonged over periods up to three years, so that they are able to go about their daily duties practically symptom-free, although we know from periodic examinations that malignant tissue is still present.

Fourteen patients only out of the entire series are now clinically free from disease for periods ranging from four months to four years. Two of these cases were granulomas of the type of lymphosarcomas, while others were typical adenocarcinomas or epidermoid carcinomas. The oldest case now free from disease for about four years has a marked fibrous tissue stenosis due to over-radiation with heavily filtered radium placed within the lumen of the gut. This error we feel we can now safely eliminate by proper protection. Another case treated over a year ago had an annular growth 6 cm. in diameter of the lower sigmoid—operation was advised against because of a high percentage of blood sugar—and following two treatments with radium he has now been entirely free from any evidence of disease for nearly a year. No stricture is palpable and the patient has no symptoms. The result is of interest because of the complicating diabetes.

A type of case that had been very discouraging to us until the past year, was the bulky infiltrating growth low down in the rectum and frequently involving the sphincter. Under radiation it appeared to improve for a time and then broke down, causing profuse discharge externally and usually with

a loss of sphincter control. Five of these cases have been treated with very large doses of both buried emanation and surface radiation followed by local excision two to four weeks later. All five cases have remained free from disease now for periods ranging from seven to fourteen months.

During the past year we have been impressed by the number of cases that seemed, for a short time, to show improvement, but were characterized later by distant metastases, usually in the liver. Under such circumstances it is quite evident that the initial discomfort resulting from intense radiation of the local lesion is not warranted if the disease has already become generalized. In view of this, we now feel that an exploratory laparotomy is justified in most instances where the local growth presents possibilities of complete regression from the use of radium. In the first place, it permits of a complete examination of the growth. If extension has taken place, it saves the patient the discomfort of an intense local treatment. If the lesion is one which warrants radical treatment with radium, it is frequently an advantage to bury emanation into the growth from above, thus insuring a much more accurate application. If a colostomy is indicated and advisable, it can be done at that time.

In a number of instances this procedure has saved the patient a great deal of useless radiation. We have been much surprised to find how frequently distant metastases were present with a relatively small primary growth. We have not depended entirely on the presence of enlarged glands to dissuade us from subsequent radical treatment, because a certain number of these are inflammatory; but in practically every instance where the glands were definitely involved the liver was also extensively involved. In these cases no radium was used locally. In some, radium and *x*-rays were used externally as a palliative measure.

We have not done a colostomy as a routine procedure. Lynch[2] feels that early colostomy in inoperable cases is as vital as early operation in operable cases. I cannot agree with either his premise or his corollary. It is quite true that a short-circuiting of the bowel relieves the growth from irritation and permits of more careful cleansing. On the other

hand, an artificial anus on the abdomen is far from pleasant. Many patients would be broken in spirit and lose their morale with the presence of such an objectionable opening. Many can be handled very efficiently and comfortably without it. I would urge a colostomy only in the case where radium application would be facilitated by it and where the possibilities of closing after treatment were good. In impending obstruction it is of course imperative. In the large group of advanced cases who can control bowel function fairly well we leave the decision to the patient.

TECHNIQUE OF RADIUM APPLICATION

The literature affords very little aid in dosage and technique of radium application in rectal cancer. Our own experience has been one of gradual change from applying filtered radium internally only, to a combination of buried emanation, filtered radium internally and externally, and, if necessary, surgical exposure in order to make the application as accurately as possible.

At first we used only one tube of 1 mm. platinum filter in rubber inserted into the stricture or packed against the lesion with gauze, where the growth did not involve the entire circumference of the gut. Following this, we used tubes of the same filtration but arranged end to end in tandem fashion, enough to extend beyond the limits of the growth above and below. These were inserted in a small rubber tube inside a larger rubber rectal tube to afford some distance: because we soon learned that the rectal mucosa did not stand radiation nearly as well as the mucous membrane in other parts of the body. This factor of irritation of normal rectal mucosa has rendered the treatment of cancer in this location much more difficult than it otherwise would be.

In 1917 we began using radium emanation interstitially. In a previous publication Dr. Janeway[8] has mentioned its use in connection with rectal cancer. This method has added more to our improvement in results than all other changes combined. It permits of distributing the radiation throughout the growth, so that an accurate approximation can be made. It permits of using both the beta and the gamma radiations,

thus resulting in a saving of radium energy. It can be introduced into the upper portion of a growth through an abdominal incision and left in situ. It permits of a continuous radiation over a period of a few weeks, thus resulting in greater dosage being possible than where filtered tubes or needles containing radium element are inserted for a few hours and then withdrawn. These emanation tubes may be inserted, by means of the usual trocar needles, through the proctoscope, or, as I frequently prefer, if the growth be low down, through a small cannula inserted alongside the examining finger. Palpation is always more important than direct vision in inserting radium emanation tubes. The tubes are about 3 mm. in length and 0.3 mm. in diameter; and so far we have observed no ill effects from them as foreign bodies. In our earlier work we used tubes of too great strength; but now we have reduced the strength of individual tubes, and can thereby get a more uniform distribution by using a greater number of tubes. At present we are using tubes of about 1 mc., although in some very bulky growths it is quite safe to use tubes up to 2 mc. in strength. One mc. of radium emanation left in situ until exhausted gives a total radiation of approximately 132 mc. hrs. Depending upon the size and distribution of the growth, our dosage of buried emanation varies from 10 to 40 mc. or a total of 1320 to 5280 mc. hrs.

It is frequently possible to introduce these tubes into the rectal tumor without anesthesia, because the pain is very slight, but I am in favor of a short gas and oxygen anesthesia in most instances. The relaxation by the anesthetic permits of a more accurate distribution of the tubes.

With the beginning use of buried emanation we fell off very sharply in the use of filtered radium internally. We soon found, however, that this was a neglect of an opportunity to get in an appreciable quantity of radiation at close range, and have resumed its use. Where the growth is annular, a string of ½ mm. platinum tubes, usually 3 to 5 is placed within the stricture. These are arranged end to end in a small rubber tube which is again encased in a larger rubber rectal tube with a metal end to facilitate introduction. They may be inserted directly or through the proctoscope. A

sufficient number of tubes should be used to go beyond the limits of the growth both above and below. Using this filtration and protection a dosage of 500 mc. hrs. per tube does not give an undue reaction. Where the growth is limited to one segment of the rectal wall a slightly different type of applicator is employed. Solid rubber rectal bougies of various sizes with two grooves cut in the side are employed. In these grooves the required number of platinum tubes in small rubber tubes are placed. Knowing the axis of the growth and its distance from the sphincter, it is possible to insert this applicator so that the tubes come in accurate and close approximation to the growth. If necessary it may be rotated in order to complete the application. This applicator has the advantage of protecting, by distance, the opposite uninvolved rectal mucosa from the full dose of radium used over the growth. We now feel that it is a distinct advantage to use an internal dose of filtered radium before burying emanation tubes throughout the growth. The surface radiation applied in this way inhibits the growth and produces at least a temporary retrograde process, during the course of which it is safer to introduce the needles carrying emanation tubes. The theoretical danger of dissemination by trauma is thereby obviated or materially lessened.

Carcinoma low down in the female rectum offers a favorable opportunity for treatment because it can be reached through the posterior vaginal wall. For this purpose we use small 2 mm. lead or brass plaques of about 4 sq. cm. surface area as the filtering applicator. One, two or three of them, depending on the individual requirements, may be placed over the posterior vaginal wall, and the other walls packed away with gauze packing. It is best to separate the plaques about 1 cm. from the posterior vaginal wall and at this distance. Eight hundred mc. hrs. per plaque with the lead, and slightly less with the brass, can be given with safety in addition to that already used within the rectum. This adjunct is of most value, of course, where the growth is low down and involving the anterior rectal wall.

At first we were disposed to apply all our treatment from within, but more recently we have been convinced that it is necessary to attack rectal cancer from every available angle,

if we are to hope for complete regression of the disease with any degree of uniformity. We have therefore resorted to heavily filtered doses of radium applied at a distance from the skin over the sacrum and, if the growth be higher up, through the left lower quadrant as well. For this purpose our usual 70 sq. cm. radium pack is used. This pack is filtered by 2 mm. of brass; and at a distance of 10 cm. from the skin 20,000 mc. hrs. of radiation can be given with safety. We feel that this adds very materially to the ultimate result.

While our dosage has always been directed toward using as much as possible with a given applicator, our technique, it will be seen, has changed very materially in the past year. We feel that with this effort to deliver as much radiation from as many avenues of approach as possible, in the cases for which we hold out a hope of complete regression, our results have been much more encouraging than with our former technique.

PRESENT CONCLUSIONS ON METHODS OF TREATMENT

Every case of rectal cancer presenting for treatment should be classified in one of three groups, depending on extent of primary growth, metastases or probability of metastases, age and general physical condition.

Group I. All cases for which a reasonable hope for complete regression can be entertained.

Group II. Advanced cases for which reasonable hope for palliative relief can be entertained.

Group III. Hopelessly advanced cases for which the physical agents hold out no chance for relief.

Such a classification is of course very vague and with further improvement in technique will be gradually changing. However, some such scheme must be employed in order to formulate a plan of treatment for each individual case.

It is reasonable to suppose that Group III will always be with us; but let us hope that with better medical education, lessening of fear and distrust on the part of the patient, and improvement in technique with the physical agents, it will be steadily reduced. For these patients with disease far advanced both locally and regionally, and with general physical condition markedly deteriorated, it is better

to do nothing except to pay attention to hygienic measures and medicinal relief. An occasional colostomy may of course be necessary, but this should be decided on the merits of the individual case.

In Group II we should give first consideration to the comfort of the patient, throughout. If surface applications of radium internally, together with radium and *x*-ray externally, will relieve discharge, bleeding, pain and obstruction and prolong life, then they should be employed with that end in view, but not pushed to the point of serious discomfort. I believe that in these cases buried emanation should be used sparingly, if at all. The reaction from it in large doses is too severe to warrant its use for purely palliative relief. In some cases a colostomy may be an urgent necessity, but as a general rule it should be left to the decision of the patient, after he has been acquainted with the facts.

In Group I we should make use of radium in as large doses as possible and through all available channels to effect a complete regression. In the majority of these cases I am convinced that an exploratory laparotomy is advisable. It can be done usually under local anesthesia with very little risk to the patient. It establishes definitely the advisability or the disadvantage of pursuing radical treatment. It frequently offers an accurate means of introducing radium emanation into the upper portion of the growth. If it is found that a temporary colostomy will facilitate treatment, it can be done at this time. In many of the smaller growths a laparotomy is not essential for localization of the disease. They can be treated very accurately through the proctoscope, and a colostomy need not be considered. In these, therefore, we can afford to count to a certain extent on the absence of regional or distant metastases. Treatment of these smaller lesions is not attended by an appreciable amount of discomfort, but I feel that we are fully justified, in the light of our present experience, in subjecting the patient to it, where there is a reasonable hope for complete regression of the disease. Emanation in sufficient amount should be distributed accurately and uniformly throughout the growth, preferably under gas and oxygen anesthesia. Filtered radium should be applied internally in every way permitted by the

anatomical relations of the individual case. Filtered radium should be applied at a distance from the skin and in maximum dosage over the sacrum; and, if the growth be high up, over the left lower quadrant as well.

In certain cases, especially bulky growths involving the anal sphincter, surgery may be employed to advantage after intense radiation.

I have made no mention of surgery for the so-called strictly operable cases. The statistics of surgery alone in these cases are before us and leave much to be desired. Unfortunately, sufficient time has not elapsed to permit of radium statistics from improved methods of application.

We feel, however, that our experience throughout this period of evolution in technique and methods of radium application warrants us in treating operable as well as some of the more advanced cases, with a reasonable hope for success.

Bibliography

1. Rennington, J. R. The end-results of operation for cancer of the rectum. *J. Am. M. Assn.*, Dec. 7, 1918, lxxi, 1892.
2. Lynch, J. M. Cancer of the rectum and pelvic colon. *J. Am. M. Assn.*, Nov. 24, 1917, lxvix, 1775.
3. Hartmann, H. *J. de chir.*, 1913, xi, 693.
4. Hartweli., J. A. The radical treatment of cancer of the rectum with particular reference to the value of inguinal colostomy. *Ann. Surg.*, Sept., 1905, xlii, 399.
5. Mayo, Wm. J. The radical operation for the relief of cancer of the rectum and recto sigmoid. *Ann. Surg.*, 1912, lvi, 240.
6. Lusk, W. C. Excision of the rectum for cancer. *Surg., Gynec. & Obst.*, Aug., 1908, vii, 113.
7. Gant, S. G. Cancer of the rectum. *New York M. J.*, July 21 and Aug. 18, 1906, lxxxiv, 111 and 319.
8. Janeway, H. H. Treatment of cancer, particularly of the tongue, tonsil and rectum, by buried emanation. *Am. J. Roentgenol.*, Feb., 1920, vii, 92.
9. Ewing, J. Neoplastic Diseases, Ed. 1, Philadelphia, 1919, 648.

V

NEW GROWTHS OF THE PAROTID GLAND

DOUGLAS QUICK, M.B. (TOR.)

This has been a very interesting and extremely satisfactory group of cases. About one-half of the series has been squamous carcinoma and the other half mixed tumors of various types.

Primary carcinoma of the parotid responds exceptionally well to radium. The growth is accessible, localized and away from important structures with the exception of the facial nerve. With the nerve the danger from the use of radium is negligible, as compared with the surgical risk in many instances. Recurrent and advanced carcinoma of the parotid, on the other hand, is subject to the same disadvantages and limitations from the use of radium as epidermoid carcinoma in any other part, of equal accessibility.

The mixed tumors afford a most interesting group. The local, visible response to radium is dependent directly on the histology of the growth. The very cellular tumors, frequently classed as endotheliomas, respond quickly and disappear entirely. On the other hand, the firm, nodular tumors in which cartilage predominates, show little visible change. Their growth, however, is stopped and they remain stationary. If anatomical conditions permit, they are best removed surgically at this stage. Another feature of the mixed tumors favors the use of radium. They are usually of slow growth and tend to remain localized. Extension to adjacent lymph-nodes is rare. Infiltration of surrounding structures is uncommon, but does occur at a late stage in some recurrent tumors. Likewise, bone invasion may occur from prolonged pressure. Necrosis with ulceration is not as common with the mixed tumors as with the carcinomas.

While the technique of treatment varies with individual cases, our general plan has been a combination of external

and interstitial radiation. The first step is a massive dose of filtered radium applied over the surface at a distance from the skin. In view of the varied histology of these growths, we have attempted to establish the diagnosis as accurately as possible by doing a biopsy in every possible instance. This procedure is made the occasion of introducing emanation tubes uniformly throughout the growth. If the tumor is obviously one with cartilage predominating we remove it entirely, where feasible.

With carcinoma of the parotid the same plan is followed with cervical nodes as previously outlined in connection with intraoral carcinoma.

Up to the end of 1920 we treated 38 cases of parotid tumors. Of these 18 were carcinomas and 20, mixed tumors.

Twelve cases were primary without involvement of cervical nodes, and the remainder were recurrent. Seven cases, all carcinomas, were recurrent both locally and in the cervical nodes. Many of the recurrent cases were advanced, following several operations, broken down and ulcerating or infiltrating adjacent structures.

Of the total group, 17 cases are now free from clinical evidence of disease for periods ranging from four to twenty-six months, the average being fifteen months. Several other cases, while not free from disease, are improving steadily.

VI

NEW GROWTHS OF THE EYEBALL AND ORBIT

Douglas Quick, m.b. (Tor.)

The large group of epitheliomas involving the eyelids and canthi will be grouped with skin lesions in general. There are, however, several smaller groups involving the eye that should be considered separately.

Epitheliomas involving the ocular conjunctiva are rare, but deserve special mention. They are usually noted early because of the aggravating symptoms produced, and they are very accessible. The great difficulty, from a surgical standpoint, in dealing with them, is the amount of scarring produced, if an adequate removal is done. In fact, it is questionable, in many cases, if an adequate surgical removal can be done without impairing or destroying vision. We have found that these lesions respond very well to unfiltered radium applied over the surface. The eye is cocainized and lubricated with vaseline to protect the cornea. The lids are separated by a retractor. A strong bulb of unfiltered radium emanation can then be applied directly over the ulcer and held in place, by means of a long handle, for a sufficient length of time to give proper dosage. This saves all surrounding parts, including the eyelashes, from radiation, and gives accurate approximation to the diseased area. Our first 3 cases were treated in this manner, but with filtered radium. While the end-results were equally good, the procedure was a more trying one for both patient and operator, the reaction unnecessarily severe and the factor of error greater than with the unfiltered bulb. We have treated 7 cases in all, with complete regression of disease in each case. The periods range from four to thirty-eight months.

Another case of melanoma in the same location was treated by radiation and surgical removal, and is now free from clinical evidence of disease ten months after removal.

One case of sarcoma of the iris treated by a combination of surgery and radium is now well twelve months after treatment.

Glioma of the optic nerve has been most discouraging in our experience. Of 12 cases treated, only 4 have shown a definite benefit from treatment. There has been checking of growth and shrinkage of the tumor, but in no case has there been a complete regression of the disease.

A rather miscellaneous group of tumors, usually lymphosarcomas or lymphomas, arising behind the eyeball, should be noted. Due to the uncertainty of clinical diagnosis in these cases, we have adopted the plan of removal of the orbital contents if an initial heavy external radiation does not produce prompt regression of the mass. This removal permits of accurate diagnosis and more intimate exposure for subsequent radiation. Of 24 such cases treated, 3 have shown complete regression of disease for periods of twenty-four to thirty months, and a number of other cases still remain well for periods of less than a year. Several temporary palliative results which we consider well worth while have been noted. The danger, however, is from extension of the disease to the various adjacent sinuses, thereby getting out of reach.

Where the disease is a straightforward lymphosarcoma, treatment of the orbital growth is usually but an incident in the treatment of the general disease, and the ultimate results are probably all the same.

VII

MALIGNANT TUMORS OF THE SKIN

Douglas Quick, m.b. (Tor.)

During the past few years, radium has come to occupy an important position in the treatment of malignant tumors of the skin. The literature on this phase of radium work is so abundant that it would seem more important to devote time to a discussion of technique than to a further consideration of its merits in this field.

Skin lesions are so readily accessible that one of the most serious handicaps in the use of radium for the treatment of malignant diseases is overcome at the outset. The three important factors to be considered are: The selection of proper filtering materials, accurate approximation of the radium to the lesion, and dosage. Of the three, perhaps accuracy of approximation is the most important factor. Skin lesions are so readily accessible that equally good results may be obtained with a wide range of filtration and dosage. If dosage be not entirely overdone at the start, it can be readily supplemented; but, unless the radium is applied accurately to the entire surface in question, failure will result. If one small portion of the lesion be under-treated, or left untreated, the disease will continue, and the result will be credited as a radium failure. We have long since passed the time when a piece of radium may be placed in the neighborhood of a malignant lesion and a favorable result expected.

The relative variations in structure of these lesions are so great that it is impossible to lay down specific rules for filtration in any particular type of growth. The operator must bear in mind the physical properties of radium and their relation to the type of filter at his disposal. He must also visualize the pathologic conditions in the individual case, and then, by judicious correlation of the two, determine

the amount of filtration required to affect the tissues well beyond the limits of the growth, with as little actual destruction as may be. It is possible, of course, to destroy any accessible lesion by the use of unfiltered radium alone; but here the effect is largely one of cauterization, and is scarcely superior to the old-fashioned escharotics. A reasonable amount of destruction, confined to the ulcerated area, is in no way detrimental, but a limit must be placed on the amount of gross destruction in the neighborhood of normal tissues. Fortunately, cancer cells have a greater susceptibility to radiation than does normal tissue, so that it is possible to destroy all the malignant cells within a given area with a minimum of damage to the normal tissues, providing proper methods are used.

We feel that we are fortunate in being able to use radium emanation exclusively. This in no way alters the procedure or renders it different from that employed by the operator using the salt itself. It does, however, afford us the advantage of a wide range of usefulness for the radium. It permits of having a large number of tubes of varying strength, and of being able to change the emanation tubes from one type of filtering tube or applicator to another without appreciable danger from breakage and loss. It is frequently found advisable to use unfiltered radium emanation. This, of course, can be done without the risk of serious loss from the breakage of a tube, such as would be entailed by an operator using a tube of the salt itself.

By unfiltered emanation we mean emanation contained in a very fine, thin, glass capillary tube filled and sealed at the ends. Since the alpha rays of radium have a penetrating power of approximately 0.8 mm. of water, it will at once become apparent that the thin wall of the glass tube removes practically all of these rays. The unfiltered tubes may, therefore, be used for the purpose of obtaining an intense beta-ray radiation with comparatively little gamma-ray effect, since the latter are very much less in amount than the former. The beta rays of radium have a penetrating power equivalent to approximately 3 mm. of water or 250 cm. in air. Water has been selected as a medium for comparison since it bears some relation to the penetration in body tissues.

By the interposition of various thicknesses of filtering metal we are able to remove a part or all of the beta rays, and, by increasing the thickness of the filters, a large percentage of the gamma rays. By visualizing the pathologic condition to be overcome as far as possible, we are able to select a filter which will afford the necessary protection against the softer rays and still permit the passage of a sufficient quantity of more penetrating rays to radiate thoroughly the area in question. While in our physical laboratory a large number of metals have been studied experimentally, in the practical side of the work we have found it advantageous to confine ourselves to a few metals of various thicknesses as filters. For example, 0.2 mm. of aluminum removes approximately 25 per cent of all radiation. This means that most of the softer beta rays are removed, but only a negligible quantity of gamma rays. Aluminum is an excellent material to use when such a light filter is required, but for greater filtration it is more practical to use a heavier metal, thereby obviating the necessity of increasing the thickness to a considerable extent. The filter which we employ more frequently than any other in the treatment of skin lesions is 0.5 mm. of silver. This removes about 95 per cent of all radiation. Practically all the beta rays are cut out, but we have left a wide range of gamma radiation. By increasing the filter to 1 mm. of platinum, 97 per cent of all radiation is excluded. Apparently this variation of 2 per cent amounts to little, but if we consider the fact that the therapeutic rays are those which penetrate the filter, it will readily be seen that there is considerable difference between the half millimeter of silver and the millimeter of platinum. With the former, 5 per cent of the total radiation reaches the tissue, whereas with the latter only 3 per cent is available, which permits the use of a much heavier and more penetrating dose in comparison to the superficial absorption produced. The variations between 0.5 and 1 mm. of platinum and between 1 and 2 mm. of platinum are so slight that they need not be considered from the standpoint of dermatologic work. The only radiation we employ which is unfiltered, in the strictest sense of the term, is an active deposit of radium prepared by exposing a thin piece of lead foil to the emanation under pressure for a

period of time sufficient to permit as large an amount of deposit as the concentration will afford. This product is unstable in that it deteriorates rapidly, but it affords a means of radiating a surface intensely, if necessary, without any appreciable deeper penetration. We have found certain uses for it which will be described later.

To summarize: We use for practical purposes in our everyday work, in addition to this last-mentioned active deposit, the so-called unfiltered or bare tube, which permits us to utilize practically all the beta and gamma radiations; a tube of 0.2 mm. of aluminum, which removes only the softer beta rays and a few of the gamma rays; a 0.5 mm. silver tube which removes nearly all the beta rays and an appreciable percentage of the softer gamma rays; and a millimeter of platinum which removes all the beta rays and a large percentage of the softer gamma rays. I have not discussed the many other filters in common use, such as lead and brass, although they are fully as good when used in proper thicknesses. We have used the aluminum because in a thickness for practical use it affords slight filtration. Silver, which, as I stated, we use most, machines readily, is easily cleaned, and its tube can be readily enameled in various colors so that one tube may be distinguished from another. The platinum we have found to be the most practical heavy metal for all-round purposes. With these types of filter we have found it possible to handle the skin work satisfactorily, and consequently have not considered it advisable to complicate matters by the use of a wider range of metals or thicknesses of metals.

As for dosage, it would be almost impossible and totally impracticable to set down any fixed rules of value for individual operators. During the past year, experimental work in our physical laboratory, under the direction of Dr. Failla, has been directed to this end; and while we hope soon to be able to place dosage on a much more scientific basis than heretofore, it is still too early, as well as outside its sphere, to make here a report on it. In the earlier part of our work we arrived at certain empiric doses after long, and in many instances painful, experience, and I daresay this experience has been shared by many other workers. The wide range of

filters used by operators in various clinics makes it doubly hard to arrive at a uniform dosage table for certain types of lesions, and the individual lesion presents so many variations that the task would be well-nigh impossible. In general, however, when the filter has been determined on, the dose should be a massive one, that is, a quantity of radiation which will produce a noticeable erythema, or even a suggestion of superficial destruction. Since silver has been our most common filter in skin work, we have arrived at an empiric unit of dosage with it, estimating it according to the extent of surface involved. With a filtration of 0.5 mm. of silver placed at a distance of 3 mm. from the surface, a unit dosage of 60 mc. hrs. per sq. cm. of surface has been our standard. If the lesion is small, that is, only 1 or 2 sq. cm. in extent, this may be increased to 70 or 75 mc. hrs. per sq. cm.; whereas, if it is much larger, the dose will necessarily have to be reduced below 60 mc. hrs. per sq. cm. on account of the cross-firing. In determining the variations in this empiric dosage, several other factors must also be taken into consideration, such as the unevenness or curvature of the surface, the type of lesion being treated or the proximity of various vital structure.

While it is of great importance to select a proper filter and consequently a proper dosage, it is of still greater importance to obtain accurate approximation of the radium to the lesion. Radiation at a distance is, of course, more uniform because the rays tend to become more homonomous the greater the distance from the surface to be treated; but this is a method of value in only a small percentage of skin lesions, to say nothing of the expense in wasted radiation. In other words, it is in most instances purely a gunshot procedure. Accuracy of approximation of the radium to the surface will always give best results with least expenditure of radium, and consequently our efforts should be concentrated in this direction.

In order to illustrate to best advantage the methods of application used, it may be well to discuss certain groups of cases more frequently encountered, indicating the type of applicator used, and adding, if necessary, a few words relative to the filtration and dosage. Our work has been confined almost entirely to the treatment of malignant lesions of the

skin, although two or three common and allied conditions have come to our attention so frequently, and have given such good results from the use of radium, that we feel it advisable to include them at this time.

Lupus of the Skin. This is a disease that we have been called on to treat rather frequently, and while I doubt if radium is as valuable in this condition as the Finsen light, the results have been fairly satisfactory. The lesion heals with a slight amount of scarring, and only in a small percentage of cases is there a tendency to recurrence. Since the disease is superficial, we have found unfiltered radium the best agent to use in its treatment. Radium emanation tubes of equal strength are placed evenly over the surface of a small wooden block 5 mm. in thickness, and over these tubes a small bit of hot paraffin is poured, which, when cool, holds them readily in place. In case the radium is to be held in place by the hand of the patient or operator, two ordinary wooden tongue-depressors may be placed together, held by adhesive plaster, and the radium tubes arranged at one end. This affords a handle by means of which the operator or patient may safely hold the radium against the area to be treated. While 5 mm. of wood removes a small percentage of the softer beta rays, the chief object is to lend distance to the application. In this way an even distribution of the radium is obtained. The area to be treated is blocked off in squares with ink, the squares being slightly larger than the applicator, so that there will be no overlapping of the radiation and consequent burning. The applicator may be changed from one of these squares to another after a sufficient dosage has been given. Using this technique, a dosage of 10 to 16 mc. hrs. per sq. cm., depending on such varying factors as the age of the patient and type of skin, has usually been found sufficient to clear up the disease with one application.

Vernal Catarrh. This is another nonmalignant condition in the treatment of which unfiltered radium has proved very satisfactory. A small block with unfiltered radium on the surface, as previously described, may be placed over each lid in two areas, so that an efficient radiation is afforded the entire lid. Provided a strong dose of radium is used in this applicator, it need only stay in place a few minutes, so that

the discomfort to the patient is slight. From the standpoint of the operator, this method of treatment is preferable because of the slight amount of exposure required. It is now, however, the most efficient and accurate method of applying radium in these cases. The active deposit of radium on lead foil, previously mentioned, is the ideal form in which to apply radium to the under surfaces of the eyelid. Lead foil, 0.1 mm. in thickness, is used, on which to collect this active deposit. After the deposit has been collected on the lead foil, the radioactivity may be measured by the same method of ionization as is used in determining the strength of our emanation tubes, and, knowing the total surface area of this piece of lead foil, we may then calculate the strength per square centimeter. The foil is then folded double so that the two surfaces covered by the active deposit are in contact. This, of course, doubles the strength per square centimeter. The folding over is done for the purpose of affording a filtration of 0.1 mm. of lead, that is, the thickness of the lead foil, for protection of the cornea. A piece of this, of the size and shape of the lesion to be treated, can then be readily cut with scissors. The eye is cocainized and petrolatum placed beneath the lid; then, with a forceps this small piece of lead foil, the inner surfaces of which are covered by the active deposit of radium, is inserted under the lid in apposition to the diseased area of mucous membrane. We always aim to have the concentration of such a degree that an applicator is required to stay in position only a few minutes. This method is entirely painless for the patient, affords a means of accurate approximation of radium to the parts to be treated, and gives the intense local effect to be desired. The only difficulty about the use of radium in this manner is the exposure of the operator. While the active deposit decays rapidly, it is, nevertheless, very intense in its effect for a short period, and since it is entirely unfiltered, the operator must be careful to keep as far from it as possible. The use of long forceps and long-handled scissors, especially if many patients are to be treated in this manner, is essential to the safety of the operator. In many cases one application is sufficient, although in some of the more obstinate cases, two, three or even four applications may be necessary.

Nevi. In treatment of nevi, or capillary angiomas, the same method of applying active deposit of radium on lead foil is the ideal technique. Except in special cases, however, it is to be avoided, because of the amount of exposure to the operator required in its preparation. Unfiltered radium on wood, as previously described, is very efficient in the treatment of most of these lesions.

Small Lesions. For the treatment of many small lesions. such as moles, papillomas or rodent ulcers, one or two small tubes of radium emanation are required. The selection of the tube and filter depends on the amount of penetration desired. For holding these tubes accurately in place, on such small lesions, we have found the ordinary red dental modeling compound used by dentists to be of inestimable value. This modeling wax, when placed in hot water for a few minutes, readily softens so that it is very pliable. A small piece of it is placed over the lesion, and the tubes pressed into place while it is still soft. In a few minutes it hardens in place and adheres to the skin sufficiently to prevent falling off. As a further precaution, in some locations, a small piece of adhesive plaster may be applied over the surface and attached to the skin at either side. This has the advantage of keeping the tubes exactly where they are placed, and prevents the movement which so often occurs if a small gauze pad is used. It frequently happens in these cases that the movement of a tube 3 or 4 mm. from the original area results in failure to obtain the desired result. We feel that it is vitally important to simplify technique in all these cases as much as possible, in order to cut down the amount of exposure to the operator, and thereby safeguard the hands of the various persons called on to handle the radium.

Treatment of More Extensive Lesions. When we treat some of the more extensive and irregular lesions, we must be more careful in our radium distribution. Success or failure will depend almost entirely on the accuracy of the approximation of radium to the involved area. In such cases we make extensive use of the dental modeling compound previously mentioned. After this wax is made plastic by immersion in hot water for a few minutes it is molded over the lesion to be treated and left in place to harden. It is then removed and

the area to be treated marked on the applicator in ink. This applicator is then taken to the laboratory and grooves made in it with a small chisel or a heated rod, so that the enameled silver tubes may be laid in the grooves at a distance of approximately 3 mm. from the surface. The tubes are so arranged that there is one tube for each square centimeter of surface. They must also be of equal strength, unless at certain points a slightly stronger dose is indicated, in which case such instructions should be marked on the applicator at the time of sending to the laboratory. When these tubes have been placed in position in the grooves they are sealed in place by pouring hot paraffin over the surface. In addition to holding them in place, this paraffin affords a sufficient filter to remove the small amount of secondary radiation from the silver tubes. I mention silver tubes because we almost invariably use 0.5 mm. silver as our filter in the treatment of this type of lesion. The applicator is now ready for applying to the growth. It will fit exactly, as the mold has been originally made so that there is no danger of applying the radium at the wrong point. The unevenness of its surface, corresponding to the irregularities of the part, prevents slipping, and it can be readily strapped in place with adhesive tape. Our dosage varies, as stated before, from 50 to 60 or 65 mc. hrs. per sq. cm. of surface, depending on the type of lesion and the amount of cross-fire encountered.

We frequently have bulky growths, in which surface applications of radium are inadequate to control the disease. Radium applied on the surface of such a lesion exerts the intensity of its effect on the least important portion of the growth. The superficial part absorbs most of the radiation, even though heavy filtration is employed, leaving the base little affected.

In the treatment of these growths we have made valuable use of buried emanation in the deeper parts of the growth, and filtered radium over the surface. This method of burying radium emanation tubes is of value in a variety of lesions coming under the care of the dermatologist. Cavernous angiomas respond favorably to their use with a minimum of resultant scar, although several months is required in which to obtain a satisfactory regression. The metastatic cutaneous

nodules of melanoma may be dissipated by burying a tube at the base, although this in no way precludes the appearance of other nodules. For the individual nodules, however, we have found it to be the method of choice.

In tabulating the cases treated during the period covered by this report, we find it practically impossible to give accurate statistical data based on follow-up of all the cases. The skin lesions have been the most difficult in our entire service to follow; and this for two reasons. First, the results are almost uniformly successful, so that the patients, with few exceptions, do not take the matter seriously enough to cooperate fully in keeping us advised of their condition. Second, the work covered by most of this report was done with limited help in the department, and, in the earlier part, with no social service, so that all available energy was directed to caring for the more serious cases.

During the four years, about 800 cases of skin epithelioma were treated. These represented all types, from early lesions to advanced recurrent ones. The basal-cell type predominated, of course, to a very large extent. In this connection one interesting feature we noted was the predominance of squamous-cell growths on the extremities. Most of the skin epitheliomas are to be found on the face, and the majority of these are basal-cell in type. Special mention should be made of the value of radium in treating these lesions in such locations as the eyelid, nose and ears, where cosmetic results are most important. The amount of resultant scarring is practically negligible unless a great deal of tissue had already been destroyed by the growth.

In the entire group of skin epitheliomas, about 95 per cent have shown complete clinical regression of disease. The majority of these results have been obtained by one application of radium. The failures in the group are represented by very advanced basal-cell cases, frequently with secondary involvement of bone, and by advanced squamous-cell growths with extension to regional lymph-nodes.

About 125 cases of various types of angiomas have been treated. Good results have been obtained in practically all cases. The port-wine stains have been most tedious to deal with, because of the danger of replacing the birthmark by an

unsightly scar. However, with care and persistence over a period of many months a satisfactory blanching with very little scarring is obtained.

Some 40 cases of lupus erythematosis have been treated. The local process responds well to unfiltered radium over the surface but the cases must be watched over a long period of time because of the tendency toward recurrence at the periphery of the old lesion.

VIII

THE USE OF RADIUM IN CANCER OF THE FEMALE GENERATIVE ORGANS[1]

HAROLD BAILEY, M.D., IN COLLABORATION WITH EDITH QUIMBY, M.A.

In the gynecological department cancer of the cervix is the chief lesion that calls for treatment and its varied form and development offer many problems in technique. Cancer of the body of the uterus, of the vagina and vulva, and occasionally of the ovary, complete the list of malignant conditions treated on our service.

TECHNIQUE FOR CANCER OF THE CERVIX

Our work began in January, 1915, with only a limited amount of radium, so that throughout that year we were able to command amounts not greater than 50 mgm. for one dose. The Continental methods then in use were copied, and consisted largely in the application of radium in heavily filtered capsules of lead. The chief factor in the technique was the application within the cervix of radium, filtered by 2 mm. of lead and a vaginal application with the lead capsule contained in a small rectangular box of tin, 3 by 2 by 1 cm. in measurement. This box was placed in the vault of the vagina and held there by a pack of gauze. In addition there were developed two methods of conveying the rays by cross-firing to the affected part: (1) A silver probe applicator was placed in the body of the uterus and held there by means of an adhesive strap band, as the wire curved over the symphysis, and (2) a lead applicator was placed high within the rectum, about at the level of the uterosacral ligaments.

[1] Read at the Sixth Annual Meeting of the American Radium Society, Boston, Mass, June 6–7, 1921. Reprinted from the *Am. J. Obst. & Gynec.*, Feb., 1922, viii, No. 2. pp. 117–133.

This was held in a T-crosspiece of rubber tubing similar to ordinary vaginal drainage tube.

While the cases falling under our care during this year were for the most part advanced, and with very slight opportunity, in any case, of effecting a cure, the fact remains that 10 per cent of those treated are well and still free of the disease. There were many cases that passed through a period of suffering from the radium effects on the bladder and rectum and there were a considerable number that developed rectovaginal fistulae. It became evident, therefore, that the technique would have to be changed so as to protect these organs.

During the year 1916, the technique was varied with this in mind, and the amount of radium at hand permitted us to use 100 mc. of emanation. The applications by vagina and rectum were largely discontinued and three applications were made within the cervix and the neck of the uterus. For the sake of convenience these applications were placed one week apart, but it was considered from the standpoint of effect as if the dose was given at one time. The filter was changed from 2 mm. of lead to 1 mm. of platinum, but the real outstanding feature of the technique of this year was that no capsule was used that was not filtered by either cervical or uterine tissue. The vagina was firmly packed with gauze, thus pushing the rectum and bladder away from the cervix as far as possible.

Although the total average dose was much higher, there was a striking difference in the comfort of the patient. Proctitis and cystitis cases became fewer in number and there were few rectal fistulae developing during the year. In outgrowing cancers of the cauliflower type, experimental trials were made with steel needles containing about 30 mc. of emanation.

The results obtained by Dr. Barringer with these needles plunged into the cancerous prostate would indicate that there might be a field for their use in uterine cancer. However, in the ingrowing types of cancer, the distorted anatomy, dilating and displacing the ureters and changing the position of the uterine vessels, would seemingly limit the field, at least for such large doses. They cause rapid disinte-

gration of outgrowing tumors, but in most instances are accompanied by deleterious effects on the vaginal wall. It is better to burn off these outgrowths with a cold cautery before implanting the radium.

The Percy Operation. During the year 1915–1916 a Percy or modified Percy operation was performed in 30 cases. The abdomen was opened, and in all instances the burning was conducted with an assistant's hand holding the uterus. In a considerable number of cases, the vessels were tied off in addition. The operation was followed by radium, the first application usually about two weeks after the operation. The results from this procedure were not good, the majority of the cases developing rectovaginal fistulae. However, there are 3 cases[1] that have remained well up to the present. In one or two patients the results following the ligature of the vessels were disastrous, leading to a sloughing of the tissues of the pelvis.

Criticism of this work would lead to the conclusion that the blood supply should not be interfered with to the extent of tying off the vessels; and further, that with the abdomen open and the uterus held in the hands of an assistant, there is a tendency on the part of the operator to burn too extensively and beyond what is advisable, if radium is to be used later. In other words, the tissue sloughed away following the burning leaves a very thin wall between the cervix and adjoining parts, and the slough which regularly follows radium dosage applicable to the treatment of cancer, breaks through this thin barrier. In later years, this form of treatment has been modified by burning away the papillomatous parts of the lesion from below without opening the abdomen and thus creating an excavation in the cervix large enough to hold the radium capsule. The radium is applied at once and a number of good results have followed this method.

The results of the repeated doses of radium within the cervix were not very good. However, during this year the cases were almost all of the advanced and the advanced recurrent types. As the cervix itself could in most instances be taken care of satisfactorily, it was found necessary to use

[1] Two cases were operated upon in the above manner in another hospital service and then transferred to us. All the Percy operations were performed by Dr. George H. Mallett, at that time in charge of the service.

some other method of radiation to affect the tissues infiltrated by direct extension and by the lymphatic invasion of the tissues in the parametrium adjoining the cervix.

The Development of the "Bomb" Technique. The application of radium placed in the vault of the vagina with the ordinary filter leads to irritation of the bladder and rectum, if the dose is above 1500 mc. hrs. Kelly and Burnam, to overcome this difficulty, placed the radium in the vaginal vault with a cover of beaten gold. They also devised a lead cup to be placed over the radium capsule, and by these methods they were able to filter the back and sides of the capsule so that very small amounts of radiation reached the adjoining organs.

In 1916, a lead capsule consisting of a small piece of lead pipe was fastened to a stiff rod so that the rays might be directed to various quarters. This idea was at once improved upon by making a small lead globe with a diameter of 3½ cm. with one pole sawed off and a set-in provided to hold the platinum capsule. This was applied with the capsule containing 1000 mc. of emanation. It was soon found that the cone of rays was too small and another apparatus was built which consisted of a thin capsule of iron. Into this mercury was poured to a depth of 2 cm. At the top of the apparatus was a receptacle with its sides protected by 6 mm. of lead and in this area was placed the radium. Over this was a 1-mm. platinum filter with a hard rubber cap. This instrument was used through the years 1917, 1918 and 1919. Radium up to 1000 mc. was placed in the container and directed first to one side, then to the center, then to the opposite side of the vaginal vault. This has been termed the "bomb" because of its almost exact resemblance to the small hand grenades used in the war. With this instrument we have been able to give 3000 mc. hrs. of radium treatment in the vaginal vault with but little irritation of the bladder and rectum (Figs. 17, 18 and 19).

We still had some trouble with rectal irritation because of the sagging of the pelvic floor due to the weight of the apparatus. At the suggestion of Dr. Bagg, a frame was built which may be placed on the patient's bed and so arranged that she is in a fixed position with her legs placed in comfort-

able leg holders. In a track in this frame is a standard with a universal ball joint at the top which holds the entire weight of the applicator and yet enables the accurate placing of it. However, even with the aid of the above-described applicator and with the radium capsule located in the cervix, the rays reaching the parametrium at a few centimeters' distance are very feeble. It is necessary to reinforce them, as far as possi-

FIG. 17.

FIGS. 17, 18 and 19. Roentgenograms showing shadows of the bomb placed directly against the lesion in the vaginal vault and against the right and left parametrium. The cervical ulcer is packed with bismuth gauze.

ble, by means of radium passing through the skin from several portals about the pelvis.

The Block Treatment. It was found by graduating the doses that 3000 mc. hrs. at 4 cm. with 2 mm. of lead and 4 cm. of wood as a filter closely approximated the skin dose when it was applied in conjunction with the other radium. The areas selected for this type of application are directly

over either groin and through the center of the symphysis on the front part of the body; against the sacrum and over either sacroiliac joint on the back. The diagram shows that each external application not only furnishes a definite radiation to a certain point in the parametrium but is reinforced by each of the other five applications. Under such combined

Fig. 18.

treatment the average case receives in all about 9000 to 18,000 mc. hrs., depending upon whether the brass or the lead block is used (Fig. 20).

In general the method outlined has been continued from 1917 to the present time, the variations being those of dosage rather than of technique. In the latter part of 1919 and up to the present time, more and more use has been made of the direct embedding of bare glass tubes containing

emanation. We have entirely confined our attempts in this direction to the small dosage, 1 mc. being the highest used and ½ mc. the average strength of each tube. The method of burying emanation tubes is particularly applicable to vulval and vaginal cancers and has some value in the treatment of recurrent cancers where there are definite nodules behind the vaginal vault.

Fig. 19.

Our Physical Department, under the charge of Dr. G. Failla, has been able to estimate the dosage administered by these various methods in terms of a skin dose (as used by us). They have also been able to measure accurately the dispersion of the rays from the front of the mercury "bomb" and from their computations have been able to build a new instrument of lead which correctly filters the sides and back to the radium and delivers in front a cone of rays of known

extent. The most practical feature of their work is the measurement of the intensity of the radiation at any point within a given area—in our case, the pelvis.

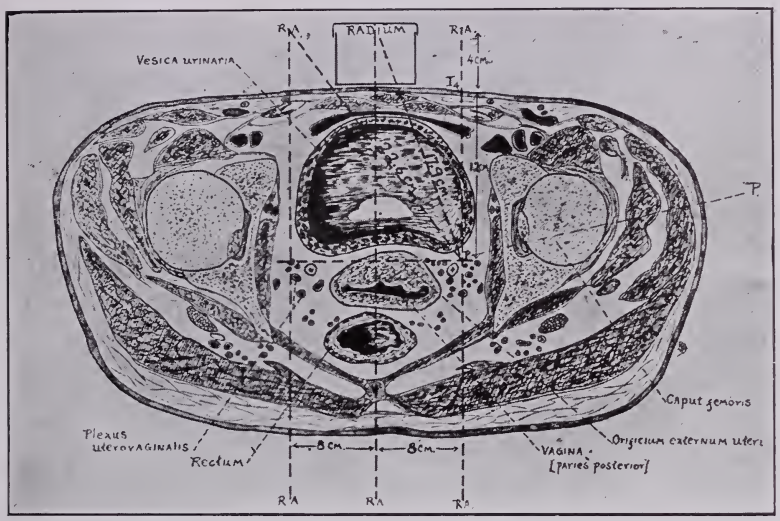


Fig. 20. Diagrammatic horizontal cross-section of female pelvis, showing small amount of tissue through which the rays pass from surface applications on abdomen and back. Point P in the parametrium about 12 cm. from either surface.

MEASUREMENT OF RADIATION

The purpose of the steel-mercury appliance was to furnish an intense beam of radiation in the forward direction and as little as possible laterally. In order to find out the actual distribution of radiation about the instrument an apparatus was constructed which gives the ionization produced by the radiation in different directions (Fig. 21). I is a conical lead ionization chamber, connected to a gold-leaf electroscope in a lead case E, by a wire passing through the paraffin-filled tube R. The bomb is mounted at B on a support which moves on a pivot so that it can be rotated through any desired angle, which is measured on a scale S. The center of the tubes in the bomb is on the axis of the support, so that as the bomb is rotated, the radiation entering the ionization chamber passes through different thicknesses of filter. There-

fore, the intensity of this radiation varies and the electroscope records this variation. Differences in intensity due to differences in distance do not enter into this experiment, since the relative positions of the source of radiation and the ionization chamber are the same throughout. Readings were taken at intervals of 10 degrees, giving a curve such as is shown in Figure 22 *A*. This is for the steel-mercury bomb. The values are based on the intensity in the forward direction as 100 per cent since we are concerned only with relative values. From this curve, we see that the intensity is much greater in a forward than in a backward direction, but still 60 per cent as much comes from the sides as from the front.

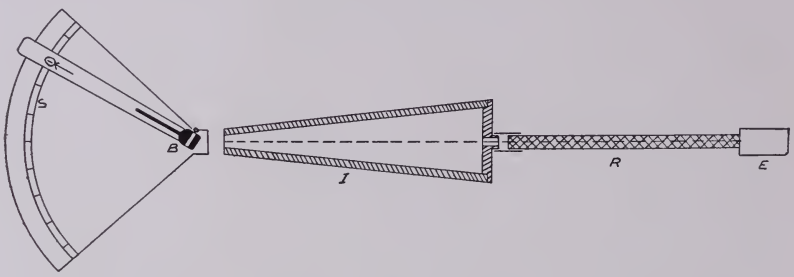


FIG. 21. Diagram of apparatus for measuring distribution of radiation. *E*, electroscope; *R*, paraffin-filled brass tube; *I*, ionization chamber; *B*, bomb; *S*, scale.

Accordingly a new bomb was designed, which is shown in Figure 23. For the protective filter lead was used, and over this a thin aluminum shell to remove the soft secondary radiation of the lead. The diameter of the bomb at the top is 3.4 cm., at the widest part 4 cm., and its total height is 4.2 cm. The rectangular pocket for the tubes is 12 mm. deep, 16 by 10 mm. at the bottom and 16 by 14 mm. at the top, so that it can hold several of the enameled silver tubes ordinarily used at the hospital. The pocket is covered by a platinum plate 1 mm. thick. Therefore the filter for the useful beam of radiation is 1 mm. of platinum in addition to the silver tubes. The purpose of a rectangular pocket was to afford as much screening as possible for the lateral radiation in at least two directions. It was intended that when the applicator was in position, these two thicker sides should be

toward the bladder and rectum, where it was desirable to have as little radiation as possible.

The distribution curves for this applicator are shown in Figure 22 *B*. It will be seen that in the direction of greater filtration, that is, toward the bladder and rectum, the intensity

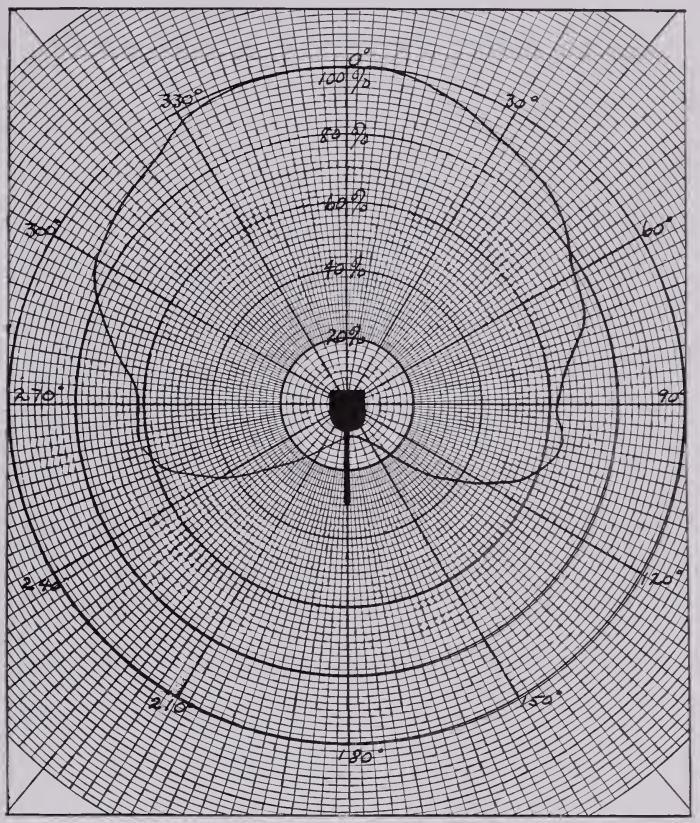


Fig. 22 *A*.

Fig. 22. Curves showing distribution of radiation about "bombs." The total radium in a forward direction is 100 per cent. *A*, Steel-mercury bomb Too large a proportion of lateral radiation. *B*, Lead bomb, with platinum filter. This is the applicator used at present.

is 30 per cent less than from the steel-mercury bomb. This lead bomb was therefore adopted for the routine treatments.

Recent experiments have shown that it is not necessary to use such a heavy filter in order to get a sufficiently pene-

trating beam of radiation for deep therapy. Filtration by 1 mm. of brass plus ½ mm. of silver has been found sufficient.[1] Therefore the bomb was tested with the platinum piece replaced by 1 mm. of brass. The distribution curves for this arrangement show a gain in intensity in a forward

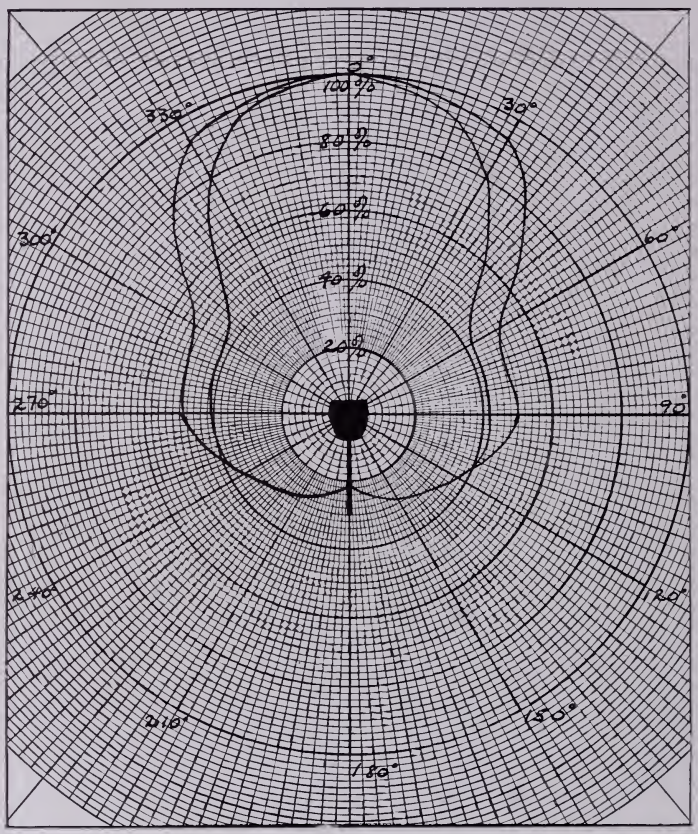


FIG. 22 *B*.

direction of about 20 per cent of the same lateral intensity. The block has also been changed so that the filter now is 0.5 mm. of silver, 2 mm. of brass and 1 cm. of bakelite. With this block we get just twice as much penetrating radiation as with the lead.

[1] Quimby, E. H. The effect of different filters on radium radiations. *Am. J. Roentgenol.*, Oct., 1920, vii, 471.

Distribution curves have also been obtained for the silver and platinum tubes in these treatments. One of these is shown in Figure 24.

The next step in the problem was to estimate the amount of radiation delivered at different points within the body, due to the bomb, block and silver and platinum tubes as used in the actual treatments. The two factors which enter into the decrease in the amount of radiation are the distance from the source and the absorption by the intervening tissues.

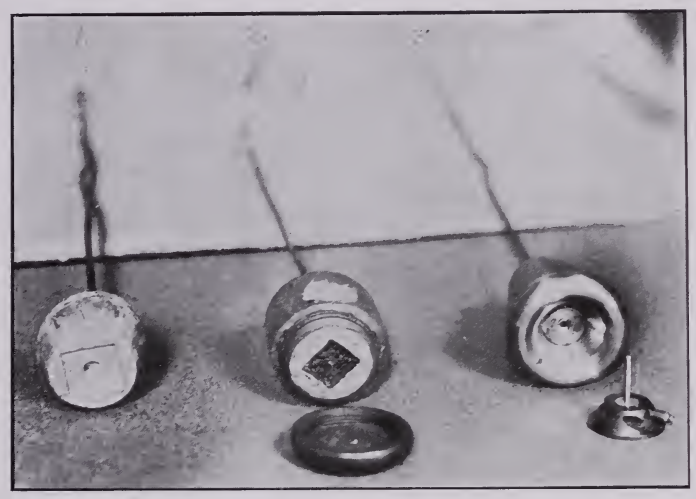


FIG. 23. Various forms of radium applicators: (1) old lead "bomb;" (2) mercury iron filter; (3) a newer mercury-iron contrivance.

The decrease due to distance was calculated according to the inverse square law, that due to absorption was obtained experimentally, and the two combined to give the intensity at different points. The density of tissue being nearly the same as that of water, the absorption is substantially the same. Accordingly measurements were made of the absorption by different thicknesses of water of radiation from these different applicators. To calculate the amount of radiation reaching different points, the percentage transmitted by any given thickness of water was multiplied by the factor expressing the decrease due to the inverse square law. For the unit of irradiation was selected the "skin dose." This is

based on clinical observations of the effect on the skin of different applicators used at the hospital for the treatment of deep-seated conditions. The "skin dose" as used at the Memorial Hospital corresponds to the irradiation from a treatment of 3200 mc. hrs. with a filter of 0.5 mm. of silver,

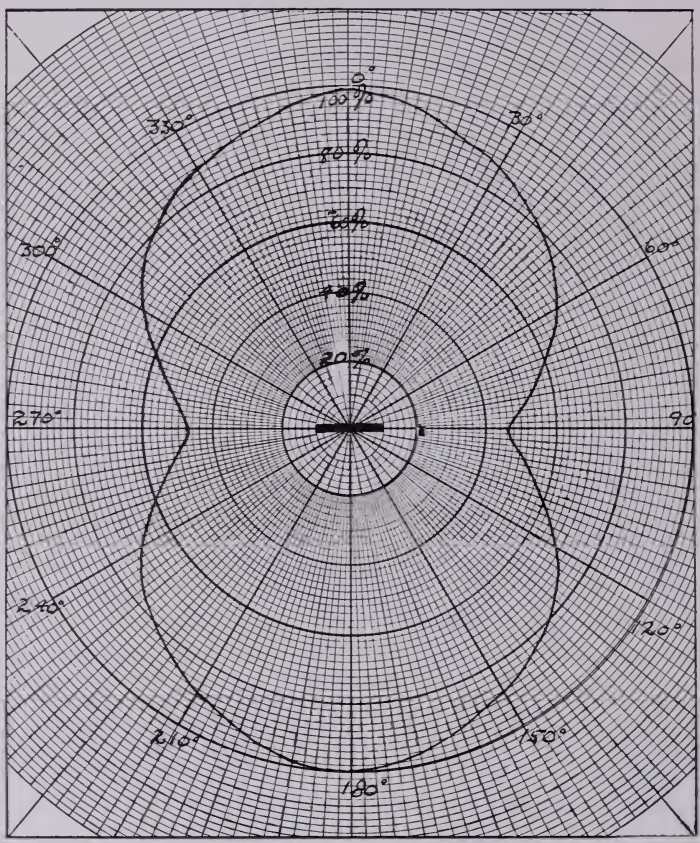


FIG. 24. Curve showing distribution of radiation about the platinum tube.

2 mm. of brass and 1 cm. of bakelite in an applicator with brass sides, the radium being 4 cm. from the skin. This is more than twice as much as can be used on patients undergoing the treatment discussed in this paper, because of the additional radiation received by the skin from the other applicators—bomb, block, tubes etc.

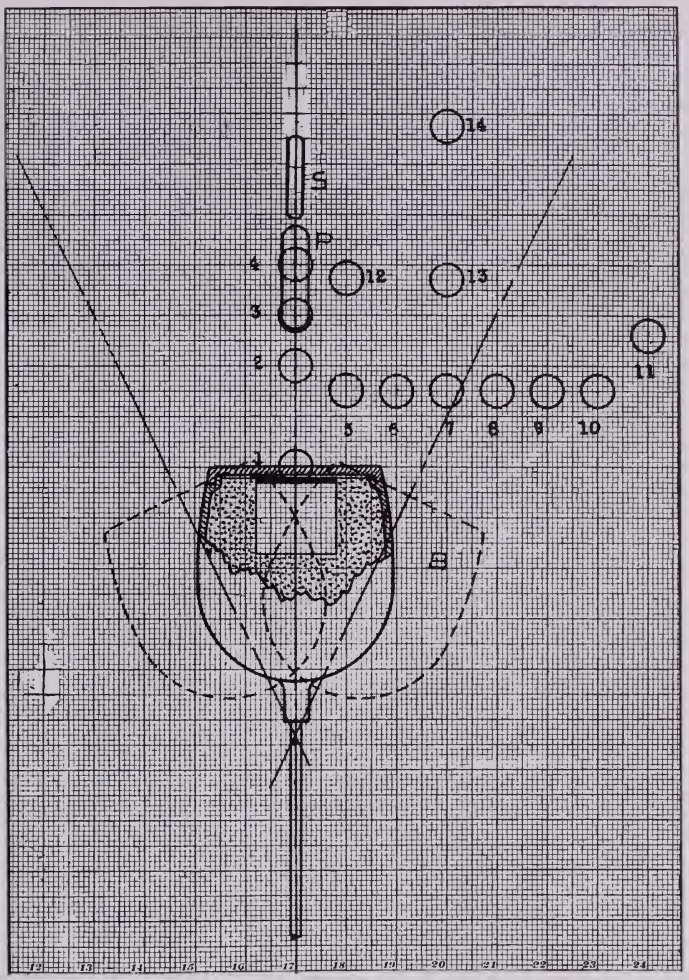


FIG. 25. Diagram showing radium "bomb" and tubes in same relation as in vagina and uterus of patient. The figures in front of the bomb are arranged arbitrarily. Table I represents the radiation in terms of a skin dose at each of these points. B, the bomb; P, platinum tube; S, silver tube. Point 1 is on the actual surface of the bomb. Point 2 is 2 cm. above. Point 3 is 3 cm. above, but also on the surface of the platinum tube. Point 4 is 4 cm. above the surface of the bomb, on the platinum tube. Points 5 to 10 represent points 1 to 6 cm. from the median line and 1½ cm. above the surface of the bomb in its center position. Point 11 is 7 cm. from the median line and 2½ cm. above the surface of the bomb. Point 12 is 4 cm. from the bomb and 1 cm. from the platinum piece. Point 13 is 4 cm. from the bomb and 3 cm. from the platinum piece. Point 14 is 7 cm. from the bomb and 3 cm. from the silver tube.

Fourteen points were taken, located as shown in Figure 25, at different positions within the pelvis, from No. 1, directly on the surface of the bomb in its median position, to Nos. 10 and 14 in the parametrium. The intensity of irradiation at each point due to each applicator, considering the bomb in three positions and the block in six, as usually used, was calculated. The results are shown in Column 6, Table I. It will be seen that the dose received by these points varies from about one-fourth of a skin dose at the most distant one considered, to several skin doses near the central applicators.

TABLE I

INTENSITIES OF IRRADIATION AT POINTS SHOWN IN FIGURE 9

1 Point	2 Silver tube	3 Platinum tube	4 Bomb	5 Block	6 Total (minimum)	7 Total (neglecting absorption)
1	0.06	0.14	2.75	0.06	3.03	3.27
2	0.14	0.62	0.41	0.06	1.22	1.83
3	0.28	64.00	0.28	0.06	65.00	65.00
4	0.66	64.00	0.17	0.06	65.00	65.00
5	0.13	0.53	0.61	0.07	1.34	2.33
6	0.14	0.41	0.50	0.07	1.11	1.60
7	0.12	0.29	0.36	0.06	0.85	1.11
8	0.10	0.19	0.26	0.06	0.62	0.99
9	0.08	0.13	0.17	0.06	0.44	0.71
10	0.06	0.09	0.16	0.06	0.37	0.54
11	0.06	0.07	0.01	0.06	0.26	0.45
12	0.71	5.6	0.18	0.06	6.54	7.07
13	0.31	0.55	0.16	0.06	1.08	1.44
14	0.43	0.18	0.06	0.06	0.72	1.02

The values represent the minimum amount of radiation delivered, no allowance being made for secondary and scattered radiation, which recent experiments have shown to be an important factor; making the dose much higher than that obtained by calculations such as these. Column 7 gives the theoretic maximum of irradiation, absorption being neglected and the only decrease considered being that due to the inverse square law. The actual amount of penetrating

radiation reaching a given point is somewhere between these two values. However, the ionization taking place at the point and producing the therapeutic effect is greater than would be indicated by these values, on account of the soft secondary radiation generated by the penetrating radiation in the tissues.

Cancer of the Body of the Uterus. The technique of the radium application in cancer of the body of the uterus depends upon whether the uterus is to be removed following the treatment. We believe that where there are no contraindications to the operation from the standpoint of the general constitution of the patient, the removal should follow the radium treatment in all cases. The extent of the disease must remain unknown because it is in a position where neither sight nor sense of touch can aid one. However, there are certain cases where, owing to age or other disability, one has to remain content with the radium treatment.

In the first instance, where operation is to follow, radium is placed in a platinum capsule within the body of the uterus, preferably in a tandem piece, so that a large part of the organ may be radiated. The dose should be a total of 3500 mc. hrs. and the removal of the organ should follow at the end of six to eight weeks. We believe that there should be no earlier removal because of possible local inflammatory effects.

After the organ has been removed, external radiation should be given by the block technique. In cases where it is known that the organ is not to be removed, beside the 3500 mc. hrs. within the body of the uterus, the "bomb" is directed toward the parametrium on either side for one hour and in addition the block is applied to six areas about the pelvic girdle.

Cancer of the Vagina and Vulva. Cancer of the vagina and vulva are both treated by buried radium emanation. The strength of each tube is about 0.5 mc. In addition, filtered radium is administered by means of the "bomb" in the vagina or by tubes placed in dental compound if the involved area is at the entrance of the vagina or on the anterior wall. The glands of the groins in vulval carcinoma are radiated by the block method, and in some instances are later removed by dissection and the open area infiltrated by

bare tubes placed 1 cm. apart. In the vaginal cancer, the external radiation is given by the regular block technique through six areas.

Recurrent Cervical Cancer. Recurrences are either behind the vaginal vault or by outgrowths in the vault of the vagina. Here again, the bare tubes, "bomb" and "block" are the methods selected. If there is a crater in the vault of the vagina a platinum capsule is inserted for not more than 1200 mc. hrs.

Table II shows an analysis of results in 600 cases of uterine cancer and in 32 cases of vulval and vaginal cancer, followed to May 1, 1921.

TABLE II

RESULTS IN 600 CASES OF UTERINE CANCER AND 32 CASES OF VULVAL AND VAGINAL CANCER

(Followed to May 1, 1921)

Radium treatment	1915	1916	1917	1918	1919	1920
Advanced primary cervix	15	24(1)	41	41(7)	69(23)	92(58)
Recurrent	18(1)	8(1)	26(2)	35(8)	43(17)	37(27)
Early, operable cervix	1(1)	3	3(2)	4(2)	9(7)	14(9)
Borderline cervix	0	3(2)	3(2)	17(5)	10(7)	12(8)
Percy	15(2)	11(1)	3	0	0	0
Ca. body of uterus	1(1)	1	0	7(3)	5(3)	5(5)
Prophylaxis						
Following hysterectomy	0	.....	2	8(6)	4(3)	10(10)
Ca. vulva and vagina	0	1	0	6	11(4)	14(8)
	50	51	78	118	151	184

(Figures within the parentheses represent the number of cases alive May 1, 1921.)

DISCUSSION OF RESULTS

From January, 1915, to January, 1921, there were 600 cases of uterine cancer and 32 cases of vulval and vaginal cancer treated with radium. The follow-up has been continued to May 1, 1921, and the figures in each group

show the total number of cases treated, with the number of those alive placed in the parentheses. In the group of the first three or four years, that is, from 1915 to 1918, the figures will probably remain as they are, for the cases that have lived through such a long period are presumably cured and their number will only diminish through death from intercurrent disease.

The follow-up is continued by weekly clinics, by visits of Social Service nurses and by letter. No case is discharged, and those lost through failure to return or by change of residence are classified as dead. We find that these patients are so thoroughly impressed by their treatment that if they do not return or continue in the follow-up clinic, the reason is usually due to their ill health caused by the advancement of the disease. There have been a few who discontinued their treatment before it was completed, but even these cases, since 1918, have been included in our lists, because in our technique, all the treatment is given in twenty-four hours. In other words, they have discontinued the follow-up observations, and not the treatment.

We feel that the technique which has been standardized since 1918 and by means of which the parametrium is thoroughly radiated, will provide us with better results than we have had in previous years. However, the number of those alive in the 1919 and 1920 groups will drop to a considerable extent, especially in the two classes: advanced primary and recurrent cancer.

Early or Operable Cancer of the Cervix. This group is the most important one and demands a few words of explanation. In the year 1915, the one case was a woman of about seventy years who had a very early cervical lesion but with the specimen showing epidermoid carcinoma. She has remained well. Of the 3 cases of 1916, one was operated upon in another clinic within a month after our treatment and died on the third day following the operation. The removed uterus showed no carcinoma. The second case died of appendicitis a few months after treatment and the diagnosis was confirmed by a visit from one of our staff. The third case, one month after treatment, had an attack of acute rheumatism and died of cerebral embolus.

Of the 3 cases of 1917, 2 are alive and the third died of cerebral hemorrhage in November, 1919, at which time there was no evidence of cancer.

Of the 4 cases of 1918, 2 are alive and 2 died from the disease.

Of the 9 cases of 1919, 2 are dead. One, in addition to her pelvic trouble, had carcinoma of the breast, and the other had a hysterectomy after our treatment was completed, and died this year of recurrent carcinoma.

In 1920, there were 14 cases in all, with three deaths from the disease. One patient was lost from our records because she gave us a false address. Another died ten days after the radium treatment following a hysterectomy in another clinic performed against our advice. Of those dying from the disease, one had a hysterectomy by us about two months after her treatment and radium was inserted in the parametrium. Notwithstanding this treatment, carcinoma developed throughout the pelvis. The second patient had a general glandular metastasis with carcinoma of the neck, axillae and the groins. The third case had an attack of typhoid fever within a month after the treatment, and although she recovered from this, her health never improved and she returned home to die.

Two of the 14 cases had negative specimens, but the clinical examinations conducted separately by Dr. Stone on the admission of the patient and by me with the patient under an anesthetic showed all the evidences of early carcinoma. It is our contention that notwithstanding the negative specimen they should be considered as early carcinoma. In the early or operable group, there are 6 cases where a valid excuse occurs for their removal from our list. If these 6 cases remain in the list there are 34 in all for the years from 1915 to 1920; and if they are thrown out, there will remain 28 cases with 23 alive. Of course it is to be remembered that in regard to the 1919 and 1920 cases very little time has elapsed. These cases are free of clinical evidence of the disease.

Borderline Cancer. Of the 3 cases of 1916, 1 is dead, although she remained well for more than four years and died of cerebral hemorrhage following an attack of pleurisy in March, 1921.

There were 3 cases in 1917. One died from the disease. Of the 17 cases in 1918, all but 5 died of the disease. Reviewing the histories of these cases it would seem that according to the classification of today, a number would not be considered as borderline but as advanced primary cases.

Of the 10 cases in 1919, 3 are dead of cancer and 7 are alive and free of evidence of the disease. One of these patients had a hysterectomy following her treatment. Of the 12 borderline cases of 1920, 4 are dead of the disease. One is in poor condition, but the others are free of clinical signs of tumor. There is a total of 45 cases during these years (1915–1920) and 24 are still alive. There are 3 cases of this group who are now clinically cured but who have rectal fistulae.

Body of the Uterus. The 1 case of 1915 is well today. One case in 1916 had her uterus removed some time after the radium treatment and carcinoma was present, the patient dying some months later. Of the 7 cases of 1918, only 3 remain alive. Of the 4 cases classified as dead, 2 dropped out of our follow-up clinic shortly after their treatment. The other 2 died of the disease nearly three years later.

Of the 5 cases in 1919, 2 are dead. One died from the disease and the other from pneumonia about six months after the treatment. In 1920 there were also 5 cases and all are alive and free of signs of disease. Of the total of 19 cases of cancer of the body that were treated throughout these years (1915–1920) 12 are alive and well.

Recurrent Cancer. The recurrent cancer forms a large group with a very high mortality. Those cases that are alive represent the early recurrent cancer where only small areas in the vault of the vagina or in the nearby parametrium were involved. The 17 cases alive in 1919 and the 27 in 1920 will be gradually reduced in numbers at the end of a few more years, for many of them still have evidences of cancer.

Advanced Primary Cancer. Of the 80 cases treated during the years 1915, 1916 and 1917, there is but 1 alive. The years 1918, 1919 and 1920, we feel will give a much higher percentage, but the 23 cases of 1919 and the 58 of 1920 that are still alive will be greatly reduced in numbers in the course of another year or two.

Prophylaxis. We come now to a more hopeful group, those that had no evidence of recurrence following hysterectomy and were treated as a prophylaxis against the return of the disease. The 2 cases treated in 1917 both developed cancer and died, but of the 8 who were treated in 1918, 6 are free of the disease. Of the 4 in 1919, 3 are alive and of the 10 cases treated in 1920, all are living. There are 19 cases in this group that are now free of clinical evidence of the disease.

Cancer of the Vulva and Vagina. This subject has been separately reported by us, and there are great prospects in this field through the use of bare weak tubes plus the filtered radium. Our results are encouraging, but as yet there is no assurance that the disease will not recur.

SUMMARY

The full technique, using the external radiation as an aid to the capsule and bomb, was not in routine use until 1918. If the advanced primary cancer and the recurrent cancer groups are taken together, there were 132 cases treated before January 1, 1918, and there are but 5 cases alive today. If these same groups are taken for 1918, there are 76 cases, and 15 are alive; for 1919, 112, and 40 are living; for 1920, 129, and 85 are still alive. While the prospects of greatly reducing these figures are present and sure, nevertheless, the indications are that in these groups we have had our greatest advance.

The follow-up of our operable and borderline classes will have to be continued through three or four more years before deductions may be made. Our present figures are remarkable and indicative.

In the prophylaxis after hysterectomy great care must be used that the tissues are not overradiated. The end-results in this class are very good for the time elapsed since treatment.

We believe that these results cannot be duplicated without the use of massive doses of radium or thorough radiation of the parametrium.

IX

VULVAL AND VAGINAL CANCER TREATED BY FILTERED AND UNFILTERED RADIUM EMANATION[1]

HAROLD BAILEY, M.D., AND HALSEY J. BAGG, PH.D.

The treatment of cancer by radium emanation, enclosed in minute glass tubes and implanted directly into the growth without any further filtration, was first suggested by Duane in 1908. Joly and Stevenson (1914) used this method and reported a series of cases so treated. H. H. Janeway standardized the procedure, using it in many types of cancer in various parts of the body. He also first made use of buried emanation as a prophylactic agent, following the dissection of lymphatic structures at a distance from the lesion. In tongue and mouth cancer, after treating the original ulcer, his procedure was to dissect the lymph glands of the neck and then imbed a number of unfiltered radium tubes. In 1919, he reported a series of 5 cases of vulval carcinoma treated by the implantation of unfiltered tubes, reinforced by filtered radium, held by dental compound on the surface of the growth.

When this method was first employed, the tubes varied from 2 to 5 mc. in strength, and in a number of instances there was considerable sloughing and irritation of the treated areas. Bagg, investigating the action of various doses of radium on living tissues, when implanted in this manner, found that the amount of tissue affected was not exponential to the size of the dose, and that, as a matter of fact, with doses from 1 to 4 mc. there was but slight increase in this area when the dose was increased by 100 per cent. However, the larger dose leads to a more intense necrosis in the tissue immediately adjoining the tube.

[1] Read at the Forty-sixth Annual Meeting of the American Gynecological Society, Swampscott, Mass., June 2–4, 1921. Reprinted from the *Am. J. Obst. & Gynec.*, Dec., 1921, ii, No. 6, pp. 587–597.

METHODS AND APPARATUS

1. *Filtered Radium.* The filtered radium is applied according to the location of the lesion by one of three methods. These methods are described in detail in previous publications and they consist in the so-called "bomb," "block" and "dental compound" applicators.

In brief, the "block" technique involves the use of 1000 to 2000 mc. of radium emanation, filtered by either 2 mm. of brass or 2 mm. of lead, and ½ mm. of silver, and held from the skin by 4 cm. of wood. In the first part of our work, lead was used as a filter and the dosage was 3000 mc. hrs. Following the research of our Physical Department, it was found that such heavy filtration was unnecessary, and an equivalent dosage was determined with a brass filter, which has resulted in a material saving of the available radium. The "block" is applied for radiating the local lesion and both inguinal regions in vulvar cancer, and is used in six applications around the pelvic girdle in vaginal cancer.

In using filtered radium applicators for external lesions we follow the method devised by Dr. Janeway, which consists in using a 1-mm. platinum capsule held in position by dental compound. The dose is usually 350 mc. hrs., the applicator being placed on the surface of the lesion. This method was also employed in treating lesions of the anterior vaginal wall.

The "bomb" was used only for the vaginal lesions. One thousand mc. of radium emanation, with a filter of 1 mm. of platinum, was used for one hour directly over the growth. This applicator is so constructed that side radiation is minimized, and the rectum and bladder are protected by a heavy filtration of lead.

2. *Unfiltered Radium.* The unfiltered radium is inserted into malignant growths by means of long steel trocars. The small glass tubes consisting of radium emanations are placed at the pointed end of the instrument, which is then thrust into the tissue and the trocar is slightly withdrawn, as the tubes are deposited, by exerting pressure on the stylet.

EXPERIMENTAL RESULTS FOLLOWING THE IMBEDDING OF UNFILTERED RADIUM

The localized reaction of the buried radium emanation is probably due to three reacting factors: First, the dispersion of the rays is increased the greater the distance from the source, so that the more distant gamma-ray effect is comparatively slight and less sharply defined than the more intense beta-ray reaction immediately surrounding the tube. Second, as shown by the recent work of Quimby, the beta rays are largely absorbed by a few millimeters of tissue. Third, the inflammatory reaction set up in the tissues in response to the radiation tends to localize the reaction. When strong tubes are used the area of tissue immediately surrounding the source of radiation is radiated for a longer time than is necessary to produce the death of the cells, and we believe that in most cases this is undesirable.

CANCER OF THE VULVA

There have been 10 cases where the labia were involved, the lesion varying from round flat growths, 2 cm. in diameter, to larger masses 1½ cm. thick and 7 cm. in the longest diameter. In most instances the lymph glands were affected. The pathological reports showed squamous-cell carcinoma, with one exception, myosarcoma. One of the cases developed a vulval tumor two years after she had appeared in the clinic for treatment for a recurrent cancer in the vaginal vault following a hysterectomy. Although only short periods have elapsed since the treatments, several of the cases have shown marked improvement, and this fact has encouraged us to continue this technique.

Outline of Treatment of Vulval Cancer. (1) Radiating the primary lesion with filtered radium. (2) Radiating the groin on both sides with filtered radium. (3) Imbedding unfiltered tubes of 0.5 mc. each, in the primary growth, placed ¾ cm. apart. (4) Dissection of the groin, when necessary, with further radiation by means of buried emanation.

In our first enthusiasm with the method of imbedding many bare tubes of weak strength, we saw such regular and

prompt retrogression of the ulcer that it seemed unnecessary to treat the lesion further. However, the marked and early involvement of the glands caused us to turn again to the primary ulcer. This was then treated with filtered radium; but recently the procedure has been reversed, and the filtered radium is used first to avoid the possibility of spreading the disease by trauma at the time of the implantation of the tubes.

Treatment of the Ulcer. In inserting the glass tubes, of approximately 0.5 mc. value, the tumor is theoretically marked off into square centimeters, and one tube is placed in each area. In larger lesions, 5 to 7 cm. in diameter, it is well to implant the tubes along the edge of the growth at about ¾ cm. distance, and, leaving the needles in place, implant the remainder in parallel lines from the edges. The needle carrier is inserted as near as possible to the base of the ulcer; and before the radium is discharged, it is withdrawn slightly as the stylet deposits the bare tube.

All the cases should be seen after three weeks, and then it will be evident what areas, if any, have been untreated or ineffectively radiated. We find that a second treatment is usually necessary.

Treatment of the Lymph-nodes. Although external radiation is usually considered as but feebly affecting glandular metastasis, we have relied upon it to the extent of first treating the groins with a dose of 3000 mc. hrs., at a distance of 4 cm., with the lead "block," or with 2000 mc. hrs. with the brass "block." After a period of six weeks or two months, if there is palpable involvement, the glandular areas are dissected on one or both sides. If the lesion is in the upper part of the vulva, the glands of both sides may be involved.

We have been satisfied with simple dissection of the inguinal chain with sometimes an additional incision over the femoral area. On removal of the glands, unfiltered tubes of 0.3 to 0.5 mc. each are laid 1 cm. apart, and if possible, also into the stump of the lymphatic chain. Bare tubes[1] have been laid in glandular masses entering the femoral ring, and also in glands above Poupart's ligament. If the

[1] Bare tubes refer to radium emanation filtered by only 0.3 mm. of glass.

radium is not laid directly against the vessel, or into its lumen, tubes of 0.3 mc. apparently do not lead to erosion. There have been no secondary hemorrhages in this location and none within two months of such insertion directly through the vaginal vault. We have had but two primary hemorrhages in the pelvis from direct injury by the needle during the insertion, and these have fortunately been readily controlled.

Where the glandular metastasis has extended into the pelvis, rather than do such a radical dissection as in Basset's operation, we have relied upon the surface application of filtered radium for palliative purposes. There have been some cases requiring a second dissection of this region. As in surgery, the primary lesion is easily taken care of, but the lymph glands bring final disaster in many of the cases.

Of the 6 cases of this group that are still living the following are selected for purposes of showing the actual experiences with the technique.

1. *Vulval carcinoma, with lymph-gland involvement, resulting in a complete retrogression of the original ulcer, and with the glandular areas held in check.* No. 27088. Age thirty-nine. Microscopic examination of specimen showed epidermoid carcinoma. Hysterectomy in October, 1918. Vulval lesion noted the following June. Examination: Lesion of the vulva extending from the urethra two-thirds of the way to the fourchette. The inguinal glands on the left side are enlarged. Treatment: December 1, 1919, the lead block at 4 cm. distance for 2998 mc. hrs. Two days later, seven bare tubes of 1 mc. each were imbedded in the vulval growth, giving a dose of 924 mc. hrs. February 24, 1920, 817 mc. hrs. were applied to the lesion by means of a 1-mm. platinum tube held in dental compound. One month later, the left groin was dissected and enlarged glands removed. Bare tubes of 0.5 mc. each were distributed throughout the wound, giving a total dosage of 462 mc. hrs. June 14, 1920, the right groin received a dosage of 2946 mc. hrs. by means of the lead block. December 29, 1920, there was no evidence of disease in the vulva and the glands showed no recurrence. May, 1921, the vulva showed no signs of cancer. There is a thick ridge of tissue in the groin.[1]

2. *Early primary cancer of the vulva, without palpable glandular involvement.* No. 27979. Age seventy-two. Microscopic examination showed squamous carcinoma. Growth preceded by itching of labia for a number of months. One year ago, a pea-sized lesion was noted in the vulva. Examination: There is a growth in the left labia minora, 2 by 3 cm. Irregular, hard, and with induration extending to the vaginal orifice. There is no palpable glandular involvement.

[1] At the time of reading this proof (November, 1921) six months after the paper was written, we found a recurrence in the right parametrium.

Treatment: August 10, 1920, twenty-six bare tubes, totaling 5.7 mc., were imbedded in the lesion, giving a dosage of 752 mc. hrs. This treatment was repeated with a dose of 887 mc. hrs. on November 1, 1920. Five days later, the groins were treated with a dose of 2599 mc. hrs. by means of the lead block. At present, there is a small area of cancer tissue at the site of the primary lesion.

3. *Primary cancer of the urethra, with glandular involvement and with a retrogression in both areas, followed by late recurrence at the original site of the lesion.* No. 27016. Age thirty-one. Microscopic examination showed epidermoid carcinoma. A growth was noted four months before admission to the hospital. The lesion was not painful, but bled easily. Examination: The entire urethra on its lower walls is infiltrated by an ulcerating growth. The mouth of the urethra is split open and forms an ulcer 1 cm. in diameter. There is glandular involvement of both groins. Treatment: November 10, 1919, both inguinal regions were treated with 2913 mc. hrs. by the lead block. The following week, eight bare tubes of 0.6 mc. each, giving a total of 1056 mc. hrs., were placed in the local lesion. On January 5, 1920, eight tubes were again imbedded in the lesion for a total of 243 mc. hrs. The tubes were of 0.2 mc. each. May 10, 1920, two bare tubes, of 0.4 mc. strength, were placed in hard nodules beneath the urethra. On August 23, 1920, ten tubes, of a total strength of 2.0 mc., and two of a total of 0.9 mc., were placed in the lesion around the external urethral meatus. At the same time seven tubes of a total of 3.0 mc. were placed in the right groin after dissection, giving a total dose of 397 mc. hrs., and six tubes of a total of 2.6 mc. strength (340 mc. hrs.) were imbedded in the groin on the left side. Microscopic examination of the lymph-nodes showed epidermoid carcinoma. In May, 1921, there was a recurrence of the tumor at the original site. Twenty bare tubes, averaging 0.45 mc. in strength, were placed in the lesion. The dose was 1212 mc. hrs. At the same time, a dose of 376 mc. hrs., in a 1-mm. platinum capsule, was held on the surface of the lesion by dental compound. At present there is a radium slough over the radiated area.

In this case, we depended entirely upon the use of unfiltered radium in the treatment of the primary lesion. We now feel that in all cases the ulcers should be first radiated by filtered radium, with a sufficient dose to affect outlying areas beyond the reach of the bare tubes implanted in the ulcer. The second point to be gained from the history of this case is the necessity of frequent observation, even though the patient may seem to be cured.

CANCER OF THE VAGINA

Outline of Treatment. (1) Imbedding of unfiltered tubes of 0.5 mc. each, in the primary growth and placed about ¾ cm. apart. (2) Filtered radium in the "bomb" applicator directed toward the growth. (3) Six external applications of filtered

radium by means of the "block," reinforcing the radiation in the parametrium.

The two following cases are selected as typical of the lesions occurring in this location.

1. *Primary carcinoma of the vagina with no parametrial involvement, showing complete retrogression.* No. 26990. Age fifty-two. Specimen showed papillary epidermoid carcinoma. Examination: There is an annular growth, 3 cm. in diameter, on the posterior wall of the vagina, with the limits sharply defined.

Treatment: October 29, 1919, six bare tubes with a total dosage of 6.6 mc. and a value of 814 mc. hrs., were implanted in the tumor. One month later this was reinforced by 1040 mc. hrs. by means of the "bomb" applicator. February 11, 1921, there was a slight thickening in the posterior vaginal wall. May, 1921, there is no evidence of disease, and the vaginal wall is elastic.

2. *Primary cancer of the vagina, with parametrial involvement, and complete retrogression.* No. 27245. Age forty-one. Specimen showed squamous carcinoma. Examination revealed a primary growth on the posterior vaginal wall, 4 by 5 by 1 cm. in diameter, extending to the vault, but not involving the cervix. The rectal wall was free, but the right parametrium was thickened.

Treatment: January 16, 1920, seventeen bare tubes, of a total of 5.9 mc., and a value of 779 mc. hrs., were imbedded in the growth. An external treatment over six places about the pelvic girdle, with a dosage of 2850 mc. hrs., was given by the lead block. Three days later, 1050 mc. hrs. were given by the "bomb" method, with the apparatus directed toward the lesion. Examination shows a slight bridge of tissue crossing beneath the mucous membrane. There was no evidence of cancer.

There were 18 cases treated by this method, and of these, 5 are alive and 4 are apparently free of the disease, although only short periods of time (the longest is two years) have elapsed since the treatment. All the growths were primary with two exceptions. These had recurrences in the lower or first portion of the vagina, following hysterectomy for cancer of the uterus.

If the growth is localized on the posterior wall, a finger in the rectum aids in fixing the indurated area and facilitates the placing of the tubes. If the growth is on the anterior wall, one or two needles are inserted into the center of the growth, about ¾ cm. apart, and after discharging the emanation tubes, they are left in the growth and the shank of the needle is grasped, thus holding the entire area in position, while the remaining tubes are inserted. In the lower third of the vagina the bare tubes are reinforced by means of radium in platinum tubes, held in place by dental compound. In the upper and

middle thirds, the filtered radium is given by means of the "bomb."

With but one exception, there have been no glandular enlargements of the inguinal region in the cases where only the vagina was involved by the primary growth. All the lesions were of the ulcerative type and were accompanied by underlying induration, which in a few cases extended into the parametrium and could be readily palpated through the rectum.

DISCUSSION OF RESULTS

Until Janeway instituted the use of imbedded emanation in vulval cancer, the general opinion of gynecologists had been that radium had no place in this field, and even recently we have seen a statement to this effect. From a study of the subject extending now for a period of more than three years, we must disagree with this opinion, for we know that the original lesion may be completely eliminated without loss of any considerable amount of normal tissue and with comparatively little pain.

We believe that the method outlined is an ideal one for destroying the primary lesion. There is a minimum opportunity for spreading the disease, especially if the insertion of the tubes is preceded by an application of heavily filtered radium, which tends to devitalize the tumor cells. Wherever possible, the radium tubes surrounding the lesion are inserted through normal tissue. It might seem at first that the cautery could accomplish as much and in a shorter time. It must be remembered, however, that the two reactions are dissimilar. The imbedded radium produces a prolonged, gradual, reactive inflammation which is effective in checking the extension of the disease.

Experience with various doses of imbedded unfiltered radium emanation has shown that if the tubes are of 5 mc. strength, the elimination of the tumor is associated with extensive sloughing and prolonged and serious discomfort; whereas the smaller dose of about 0.5 mc. accomplishes as much for the removal of the growth, but without sloughing and with little pain. Except in the most minute lesion, it is not possible to arrange the placing of the tubes so that all

the cancer cells are effectively radiated. Filtered radium to check further the growth of the injured or partly damaged cells, is necessary as an adjunct to the implantation of bare tubes in vulval and vaginal cancers.

Bibliography

Janeway, H. H. *Surg., Gynec. and Obst.*, September, 1919, xxix.

Bagg, H. J. The action of buried tubes of radium emanation upon normal and neoplastic tissues. *Am. J. Roentgenol.*, 1920, vii, 536.

Quimby, Edith. The effect of different filters on radium radiations. *Am. J. Roentgenol.*, 1920, vii, 492.

Joly and Stevenson. *Proc. Roy. Soc., Dublin*, May 1, 1914.

X

FOLLOW-UP RESULTS OF 908 CASES OF UTERINE CANCER TREATED BY RADIUM

HAROLD BAILEY, M.D., AND WILLIAM P. HEALY, M.D.

We have used radium in the treatment of uterine cancer at the Memorial Hospital for over eight years, and from time to time have reported the results. In May, 1921, at the last presentation, it was apparent that there was considerable improvement in the results of the second three-year period, and we ascribed this improvement in the years 1918–1920 to the difference in our methods of treatment. To some extent this still holds good. In the first three years, 1915, 1916 and 1917, the treatment was conducted with only a limited amount of radium and its application was localized, as in the Continental procedure. At the end of the year 1915, our attempts to cross-fire through the rectum and through the uterus were discontinued because of the frequency of rectovaginal fistulae.

The technique adopted in 1916, of which we still approve from the standpoint of those operators using amounts comparable to 100 mg., consisted of the reapplication of the radium to different areas in the cervix. For the first week 1200 mc. hrs. were used, for the following week the same dose and for the third and fourth weeks slightly smaller doses. This always leads to a deep slough in the cervix, but it concentrates the radium in the center of the disease.

In some 30 cases, use was made of the Percy operation with the radium application two weeks after the burning, but it was finally given up because the majority of the cases developed fistulae. Of the 30 Percy cases, 1, treated in 1915, is well today. Another patient, burned by Dr. LeRoy Broun and sent to us in 1915 for radium treatment, is well; and a third, who had two cauterizations and was later treated by us in 1916 was well at the time of writing this report. How-

ever, we believe that the interference with the blood supply in addition to the cauterization and the tendency of the operator to burn too extensively, together with the thinness of the barrier for filtering the radium that is afterwards applied, render the operation inapplicable in most cases.

From the year 1918 to date we have made great use of cross-firing from the vagina, from the neck of the uterus and from the external surface of the body; and practically all our cases have been so treated during this last period of five years.[1] The particular method developed was the use of a platinum piece in the cervix with another above in the neck of the uterus for a total of about 3000 mc. hrs., and the radiation of the parametrium by a gram or more of radium placed in the vault of the vagina, in the so-called bomb container. This container is directed toward each lateral fornix in turn, with a central application against the cervix to reinforce the radiation in the tissues immediately adjoining the cervix. The external application was given by radium on a block applicator placed in six different regions around the pelvic girdle, half of a skin dose being given in each place. We found that when a full erythema dose was given with additional irradiation from below, the skin area would be severely burned. Lately, that is, in the past year, we have substituted for the block, which gives only a small dose deep in the pelvis, *x*-rays, with prolonged and intensive application. We believe that some form of external irradiation is necessary and advisable in most cases.

Our technique with the *x*-ray has been to give the irradiation through four areas, two on the front and two on the back of the body, and so arranged that the entire skin surface over the pelvis is covered. Two tubes working simultaneously and so placed that the rays converge toward the center of the pelvis result in considerable cross-firing beneath the skin surface. The first application is for fifteen minutes, and the second occurs forty-eight hours later for the same length of time. The filter is 5 mm. of aluminum, the focal distance 12 in., the spark-gap 10 in. and the kv. 90 to 110 with 5 ma. of current. The additional irradiation thus provided is of con-

[1] Bailey, Harold and Quimby, Edith. *Am. J. Obst. & Gynec.*, Feb., 1922, ii, No. 2.

siderable value in the treatment of the areas involved by cancer that are some distance from the cervix and vaginal vault.

The follow-up has been particularly difficult. In the earlier years we were working in a new field, and the length of time of the action of the radium, the depth to which efficient irradiation is carried and the later results from the production of fibroid tissue were all unknown to us, and these patients had to be brought in very frequently for observation. As the years passed they were asked to return to conferences for the instruction and information of visitors. After four or five years of this frequent following and control, the women objected decidedly, and in a few instances it is now impossible to get them to come back. Some even seek to avoid observation and recall by refusing to answer letters and moving to new addresses without informing the hospital. A very personal request is necessary for those who have been more than five years in the follow-up service; a nursing call or letter is rarely effective. However, without the Social Service workers, we would be in a very poor position to continue our work; their energy and tact have helped to make this report possible. Most of the cases of the first four years have been seen by us, but from a number of them we have accepted, as evidence of their present condition, either a personal letter or a letter from their physician, stating that their health was satisfactory. Those cases that have been lost, and there are quite a number of them, have been accepted as a charge against us; in other words, they have been considered as dead. Occasionally, after one of these reports, a case which has been placed in the final list returns, but this is unusual and does not interfere to any extent with the statistics.

We shall first take up the discussion of *advanced primary cervical cancer*. Of course, in this group there was very little hope of producing a cure under any circumstances. When the treatment was undertaken, not only was the cervix involved, but the parametrium as well. In the first two or three years all the advanced cases were treated, whereas now we limit ourselves to those cases in which there is apparently an opportunity to irradiate beyond the outlying part of the

tumor growth. We are averse to treating very advanced cancer with radium, even with the so-called palliative treatment. It seals up the surface of the growth and there is no outlet for the broken-down areas beyond. To give a heavy treatment such as we use in the other cases to one of these women produces a condition of pain and distress beyond description.

The advanced primary cancer forms the largest group of our patients. If we take the first three years, 1915, 1916 and 1917, in which the radiation was without any decided amount of cross-firing, there were in all 80 cases, and but 2 women are alive. In 1918 with the use of the bomb and block, there were 41 cases, and 6, or 14.5 per cent, are alive and free from the disease today. In 1919 there were 69 cases, with but 5, or 7 per cent well, and 2 alive with the disease progressing. In 1920 there were 92 cases, with 8, or 8.7 per cent, alive showing no evidence of cancer, and 7 alive with symptoms.

In 1921, there were 85 cases, and 12, or 14 per cent, have now no evidence of the disease, with 19 in various stages. In 1922 there were 80 cases and 12, or 15 per cent, are apparently well, and 45 others are alive. While not enough time has elapsed since the treatment of the cases of the last two years to give any idea of the final results, still, of the 165 cases that were beyond the aid of surgery, 24 now show no clinical signs of cancer.

Borderline cervical cancer really laps over into the advanced group, and the line of demarcation is a clinical one and largely influenced by the personal equation of the examiner. In general, in our opinion, these cases were not suitable for surgery. *In the first five years* there were 33 cases, of which group 8, or 24 per cent, are alive. All but 1 of these are known to be free of evidence of the disease. In the last three years there were 51 cases, and of these there are 22, or 43 per cent, with no evidence, while 15 show the presence of tumor tissue.

In the *early operable group* there were 11 cases treated previous to January 1, 1919. Of these, 3, or 27 per cent, are alive and free from evidence of cancer for five years or more. If the rate is corrected by deducting 3 deaths from intercurrent disease and 1 following operation in another clinic, the result is 43 per cent clinically cured for the period. During

the last four years there have been 48 cases, and of these 32, or 66 per cent, are free from evidence of the disease. If we are permitted to deduct 3 cases, 1 dying after an operation in another hospital a week after our treatment, and 2 others giving false addresses so that they could not be followed, there are 32, or 71 per cent, alive of 45 cases. In these early cases we naturally look for and hope to get excellent results from irradiation, and very few of our cases receive any other treatment.

However, there seems to be no doubt that hysterectomy alone has cured cases of cancer of the cervix. For that reason it may, at times, be considered advisable, in very favorable cases, to follow the full irradiation treatment by an abdominal hysterectomy some weeks later, so that the patient will not be deprived of any advantage which may accrue from such procedure. Just how much is to be gained by this is still a matter of conjecture.

Recurrent Cancer. Previous to 1918, there were 52 cases. Of these 2 are alive and well and 1 other is alive but with some evidence of tumor. In the past five years, during which time the technique has been considerably elaborated by the use of cross-firing and the embedding of radium emanation in the lesion, a remarkable number of these cases has been apparently cured. There were 168 cases in this group, and 38, or 22 per cent, have no clinical evidence of cancer.

Prophylaxis Following Hysterectomy. This is a very interesting group made up entirely of cases referred by various operators soon after abdominal panhysterectomy had been done in each case. In no instance was there any evidence of cancer when the patient presented herself to us for treatment; therefore it seemed probable that the best procedure would be to irradiate the entire pelvis by means of cross-firing with the bomb placed within the vagina, and the radium block, or more recently the *x*-ray, for deep external radiation. There were 29 cases between 1917 and 1923, and of these 21, or 72.5 per cent, are alive and well and have remained free from any sign of recurrence; and 5 have been well for five years.

Cancer of the Body of the Uterus. We have had 41 cases of this type, of which 21, or 49 per cent, are alive and well.

Three of these have passed the five-year period. Nine of the 21 cases had hysterectomy following the irradiation. In the other cases hysterectomy was not considered advisable because of the other complications or constitutional diseases, and these cases have been treated by irradiation alone. The plan followed was the introduction of radium into the uterine cavity for 3000 to 4000 mc. hrs. with light filtration, and external radiation with *x*-rays. Despite this treatment, in nearly every instance subjected to irradiation only, evidence of the disease reappeared within a year.

These results, we believe, are sufficiently encouraging to be worthy of careful consideration. It is our opinion that they could not have been obtained without the use of massive doses of radium and without thoroughly radiating the parametrium.

FOLLOW-UP OF 908 CASES OF UTERINE CANCER TREATED BY RADIUM TO JANUARY 1, 1923

	Advanced primary cervix	Borderline cervix	Early operable cervix	Recurrent	Body of uterus	Prophylaxis after Hysterectomy	Percy
1915	15	0	1 (1)	18 (1)	1 (1)	0	15 (2)
1916	24 (1)	3 (0)	3 (0)	8 (1)	1 (0)	0	11 (1)
1917	41 (1)	3 (1)	3 (1)	26 (1)	0	2 (0)	
1918	41 (6)	17 (5)	4 (1)	35 (4)	7 (2)	8 (6)	
1919	69 (11)	10 (2)	9 (6)	43 (5)	5 (1)	4 (3)	
1920	92 (14)	12 (3)	13 (4)	37 (14)	5 (3)	10 (8)	
1921	85 (31)	12 (9)	10 (8)	24 (14)	9 (8)	3 (3)	
1922	80 (57)	27 (26)	16 (16)	29 (25)	13 (12)	2 (2)	

Figures within the parentheses represent the number of cases alive January 1, 1923.

XI

TECHNIQUE AND RESULTS IN THE TREATMENT OF CARCINOMA OF THE BREAST BY RADIATION

BURTON J. LEE, M.D.

As a part of the organized effort which has been carried on for several years at the Memorial Hospital, for the study and treatment of malignant tumors in their many and varied phases, a breast service was organized in 1919, to concentrate under a single head the work in this field.

It has been my privilege to be responsible for this service, and the present paper presents a brief summary of the technique employed and the results accomplished up to the present time.

The cases under report were admitted to the hospital in the years 1918, 1919 and 1920, and none of our cases of the last year and a half have been included. We believe that too often, radiation is thrown into disrepute as a therapeutic agent by over-enthusiastic reports of brilliant recent results. Certainly any form of treatment applied to cancerous disease must stand the test of considerable time to determine its real value; and radiation is no exception to this rule.

Further, a record of the exact status of the case at the time of admission, with continuous notes of observation and treatment are useful, if one is to estimate what really has been accomplished.

TECHNIQUE

X-Ray Treatment. There has been an evolution in the *x*-ray treatment of breast cases during the past few years at the Memorial Hospital. Up to the present time, all treatments have been given by the ordinary type of *x*-ray machine, delivering a peak voltage of approximately 90,000 volts. Some years ago the exposures were of three or four minutes each, with a spark-gap of 8 in. and a focal distance 8 or 9 in., using 4 ma. of current and 4 mm. of aluminum

filtration. These exposures were given at varying intervals, usually four or five weeks apart. Eventually definite telangiectases appeared in the radiated skin, and in one or two instances, definite epithelioma developed in the site of the overradiated area.

Three or four years ago the time period was lengthened to six or seven minutes with a spark-gap of 10 in. and a 10-in. focal distance, with intervals between the treatments of about five or six weeks, the number of treatments given over any one area usually not being more than three or four. This type of radiation has undoubtedly given a more penetrating effect; the skin becomes definitely pigmented, but up to the present time but few cases have shown marked telangiectic areas.

Within the last year, stimulated probably by the recent work with high-voltage machines, the time period has been increased from fifteen to eighteen minutes and longer, with a 10-in. spark gap and a 12- to 15-in. focal distance, using 4 ma. of current and 4 or 5 mm. of aluminum filtration. This type of treatment has been used where the tumor of the breast was of considerable thickness and a definite radiation of the deeper tissues was desired. Where superficial subcutaneous nodules were being cared for, the older type of radiation with five- or seven-minute exposures has been the usual procedure.

We have used the *x*-ray routinely as a preoperative treatment before a radical operation, giving one complete cycle of about four treatments over the whole breast, axillary and supraclavicular regions. Following operation, after the wound has completely healed, usually in two or three weeks, it has been our practice to give two complete *x*-ray cycles covering the whole breast and drainage areas. We feel certain that unless a very definite and pronounced erythema of the skin is produced following *x*-radiation, a tumor lying in the deeper portion of the breast has not been sufficiently radiated.

Treatment by Radium. Treatment of breast carcinomata by radium has been carried on at the Memorial Hospital by one of five separate methods of application or various combinations of them, namely: (1) pack, (2) tray, (3) dental

mold, (4) insertion of bare emanation tubes, (5) the insertion of a platinum needle containing radium emanation.

1. The pack has been described by various members of the Memorial Hospital staff, and therefore I need not go into details concerning its construction. Suffice to say it provides a filtration of ½ mm. of silver and 2 mm. of brass, and for ordinary breast tumors and axillary nodes it is placed at a distance of 6 cm., maintained by a wooden block beneath the pack, giving a dosage of 8000 to 9000 mc. hrs. over an area of approximately 70 sq. cm. This is particularly of use, we believe, in breast carcinomata involving the chest wall and sternum, small tumors of the breast itself, and over the axillary and supraclavicular region, particularly if the nodes are deeply placed. We make use of it also in metastases over bones with a similar dosage, and in spinal metastases at a distance of 10 cm., we give approximately 16,000 to 18,000 mc. hrs. of treatment, with considerable relief of pain in some instances.

2. The tray is a smaller external applicator giving the same filtration, but used at a distance of 3 cm. for more superficial and localized nodules, the dosage reaching 2500 to 3000 mc. hrs. We have found as our work has developed that we are using the tray less and less, for the larger drainage areas, such as the axillary and supraclavicular regions often contain deeply placed nodes which are more efficiently radiated by the pack than by the tray.

3. The dental mold, carrying silver-filtrated radium, we have used in a number of cases of Paget's disease of the nipple with a very limited lesion present, and in one or two instances in small inoperable carcinomata placed exactly at the junction of the chest wall with the breast—the mold fitting nicely over the carcinomatous mass. Radiation by these means has recently given some very satisfactory results.

4. The insertion of emanation bare tubes by means of a long needle carrying a plunger is being made use of very extensively in primary inoperable tumors, giving a dosage of approximately 1 mc. per c.c. of tumor tissue. Caution should be exercised that the bare tube is not placed nearer to the skin than 1 cm.; otherwise it may cause an area of ulceration. Also, one should be careful to avoid placing the bare tube

directly against a rib or rib cartilage, because of the possibility of injuring the periosteum. The general tendency in earlier years was to give repeated treatment by bare tubes in small doses. The present technique consists in carefully estimating the exact size of the tumor at the time of the original visit of the patient and making an effort at the time of the primary treatment to accomplish a complete radiation of the tumor; always, however, after an *x*-ray cycle has been given. In some instances now under observation, we believe no second introduction of bare tubes will be necessary in the breast tumor itself.

Localized subcutaneous nodules in the chest wall may be cared for also by the injection of small bare tubes of 1 mc. strength beneath the nodule; but they may also be equally well, if not better, treated by *x*-radiation. The introduction of bare tubes into axillary nodes has turned out to be a difficult matter to handle, for without opening the axilla one cannot accurately localize the node at the time of introduction, and so a satisfactory implantation may be impossible. We find often, if we open the axilla in the endeavor to isolate nodes, that it is easier to dissect fat and nodes themselves, than to attempt to introduce radium into the separate nodes.

More recently we are placing bare tubes along the inferior posterior aspect of the pectoral muscle, believing that a reasonably efficient radiation of the axilla may be accomplished by this means. Bare tubes should never be placed nearer than 1 cm. to the branches of the brachial plexus, as an intractable case of neuritis may ensue.

In general we have found the management of axillary nodes one of the big problems in the treatment of breast carcinomata by radiation; and we feel that our present method of attack is not wholly satisfactory.

5. Within the last eight months we have been using the platinum needle, giving a filtration of $\frac{4}{10}$ mm. of platinum, carrying radium emanation tubes of about 60 to 70 mc., giving a dosage of 50 mc. hrs. per c.c. The theoretical difference between this needle and bare tubes is that no foreign body is left in the tumor and a less accurate implantation is required. We have had some recent interesting regressions in tumors treated with this method, but have not

sufficient data at present to make a satisfactory report upon the results obtained.

Pleural and mediastinal involvements have up to date not been completely radiated; for the necessity of radiating normal tissue and the length of time required have made it difficult to accomplish. We are hoping that a treatment of the chest areas with our new high-power machine may give more satisfactory results in the pleural and mediastinal areas.

RESULTS IN VARIOUS GROUPS

Primary Operable Carcinoma of the Breast. Following radiation of a breast carcinoma, a definite fibrosis occurs in and about the tumor, but the mass present may not contain any definite living tumor cells. In a case which has shown considerable regression, if radiation is persisted in, and especially if bare-tube insertion or the platinum needle is employed several times, one is very apt to break down connective tissue in and about the tumor, causing an intractable ulceration. It is much wiser to avoid overradiation of such cases, being satisfied with a fair rather than a perfect result.

The average routine case in this group is given a preoperative *x*-ray cycle, followed three to four days after treatment by a complete radical operation, using the Willy-Meyer-Halstead technique, both muscles being removed. A very long oblique incision is made, running 2 in. below the costal margin, and this usually enables complete closure of the wound. Very careful and wide dissection of fat and fascia underlying skin flaps is, however, made. We have had but few examples of skin recurrence in the clinic in the past three years, so that we feel that this type of operation without a wide sacrifice of skin, is justifiable. When the wound is entirely healed, two or three weeks following operation, a complete postoperative cycle of *x*-rays is given. The case is followed routinely in the breast clinic indefinitely, month by month, and treatment is given as indicated.

Exceptional cases occurring in the primary operable group are the women at or above seventy years of age. This special group we have determined to follow through entirely on the basis of treatment by radiation. Although some older women

are perfectly good operative risks, we feel that this is a justifiable procedure in these cases, and we are following this limited group with a considerable degree of interest. Further, we believe that a definite obligation rests upon Memorial Hospital to develop data of this sort, and we believe that it is possible without added risk to our patients. We have had some very interesting and satisfactory results to date, over a period, in some cases, of two years. The procedure for such cases is *x*-ray externally, and insertion of bare tubes into the tumor and axillary masses. We do not, however, feel justified in making a further report at present on these cases.

Primary Inoperable Carcinoma of the Breast. This constitutes one of our large groups. It certainly is one in which, without radiation, a practically hopeless result must be expected by the surgeon. Of the 83 cases occurring in this group in the period covered in this report, 26 were very advanced cases, the average duration of life after treatment approximating four months, with a total average duration of two years and nine and two-tenths months. All the cases in this group are dead. Of the 57 more favorable cases, which might reasonably be treated with some hope of success, 25 are alive at the writing of this report. Twelve are doing badly and 13 are doing well. Of those doing well, the average duration of life after treatment was two years and three and one-tenth months, the longest duration after treatment being four years, and the shortest one year and five months.

Recurrent Inoperable Carcinoma of the Breast. In this, our largest group, the surgeon must look to the radiologist for definite help, for treatment by radiation offers practically the only hope of checking the disease or curing the patient. In the years 1918, 1919 and 1920, but 6 patients presented themselves to the hospital whom we felt justified in classifying as recurrent operable carcinomata of the breast.

In the treatment of these cases, *x*-radiation has been by far the agent most often employed, the radium pack or radium bare tubes being used in well-localized, sharply defined recurrent masses. In comparing our series of recurrent cases, covering three years, with those of another New York hospital where no radiation was used after operation or for

recurrence, we find that our period of life following recurrence was three times as long as theirs. We feel, therefore, that the treatment of recurrent cases by radiation gives, without doubt, a marked prolongation of life. In our group of recurrent inoperable cases we have felt it wise to make a subdivision between the really advanced cases and those in whom reasonable hope of improvement might be expected from radiation. Excluding the very advanced patients, we have had 124 cases in the recurrent inoperable class, of whom 31 are alive, some of them doing well. We therefore are greatly encouraged in the treatment of these cases by radiation.

Prophylactic Cases Reported for Treatment after Radical Removal of the Breast for Carcinoma. We have routinely given a preoperative *x*-ray cycle for the past four or five years. We believe that it is of definite sevice, and that it does not materially interfere with wound healing. Sufficient evidence has not accumulated up to date, to determine whether the preoperative cycle prevents or delays a possible recurrence, but we believe that it may do both. A later study comparing a large group of cases in which a preoperative cycle was not used with one at Memorial Hospital in which it was, may furnish some data to settle the question of usefulness.

Concerning the postoperative cycle, we feel certain that it is efficient and that it has given marked results in cases where it has been employed, for we know it lengthens the time between the operation and recurrence. We believe, too, that it may entirely prevent a recurrence if properly planned and administered, and delay the rate of growth when recurrence has already occurred.

BIOPSIES

As to the histology of cases under our care, we have made an earnest effort to obtain microscopic sections of as many cases as possible in the clinic. At present, however, we possess this information in only about 40 per cent of the cases. Up to the present it has been difficult to correlate the histological picture with the clinical behavior of the disease, although certain anatomical types follow certain more or less fixed clinical courses. We hope that by observation and study we

may reach a more reasonable basis of therapy for the various anatomical varieties of breast carcinoma.

CONCLUSIONS

All in all, the outlook in the treatment of carcinomata of the breast by radiation is a most encouraging one. We feel that in no case of mammary cancer treated by surgery can the proper use of *x*-ray radiation be discarded. Radiation properly administered is the most effective aid in the care of a carcinoma of the breast surgically treated; and in every surgical clinic a preoperative and postoperative cycle is to be employed if best results are to be obtained.

As to the treatment of primary inoperable and recurrent cases, we feel that our best method at present is external radiation by *x*-rays, with a fifteen-minute exposure, 10-in. spark-gap and 12-in. focal distance, with 4 mm. aluminum filtration and 4 ma. of current, with an implantation of radium bare tubes into the growth, giving a complete dose at the first sitting. We are greatly encouraged at the present outlook.

We know that surgery has something very definite to offer for the relief of carcinoma of the breast, but we also feel that a careful follow-up of these cases in the surgical field may reveal a much poorer percentage of five-year cures than is generally believed. Our own conviction is that of 100 cases treated surgically, 15 to 25 per cent may be expected to be alive at the end of five years.

With such a discouraging outlook afforded by surgery, therefore, we feel that the addition of radiation to the treatment of this terrible disease should be followed in a most careful and systematic manner, the radiologist and the surgeon working together to solve its therapy.

XII

TREATMENT OF RECURRENT INOPERABLE CARCINOMA OF THE BREAST BY RADIUM AND ROENTGEN RAYS[1]

BURTON J. LEE, M.D.

Every case of carcinoma of the breast may be classified in one of five clinical groups: (1) primary operable; (2) primary inoperable; (3) recurrent operable; (4) recurrent inoperable; (5) prophylactic. The last comprises patients referred to us following radical operation of the breast for prophylactic irradiation, there being no obvious evidence of cancerous disease at the time of their admission.

The present paper is a study of recurrent mammary cancer treated in the breast clinic at the Memorial Hospital during the years 1918, 1919 and 1920, comprising a series of 218 patients, practically all of whom have been completely followed up to the present date.

We have included none from the 1921 group, as sufficient time has not elapsed to warrant reporting the results of treatment. The object of this paper is to determine whether or not radiologic treatment of recurrent carcinoma of the breast is justified by the results obtained in this clinic.

Most of the recurrent cases were inoperable at the time of their admission to the clinic. In the recurrent breast group, only 6 patients have presented themselves, in the years 1918, 1919 and 1920, who could fairly be classified as having operable cases. A small, nonadherent skin lesion, or a small movable node, low down in the axilla, may properly be considered operable, if no other evidence of disease is to be found. Under these circumstances it is a correct procedure

[1] Read before the Section on Surgery, General and Abdominal, at the Seventy-third Annual Session of the American Medical Association, St. Louis, Mo., May, 1922. Reprinted from the *J. Am. M. Ass.*, Nov. 4, 1922, lxxix, 1574–1576.

to excise the recurrent nodule, irradiation being given both before and after operation. With the presence of several such lesions, however, one must conclude that the disease is probably widely disseminated, and any thought of operative relief must be discarded. In this event, irradiation is the type of therapy that must be relied on.

A considerable number of cases, namely 94, were so far advanced at the time of admission that they were obviously hopeless from the outset. The very advanced breast recur-

FIG. 26. Recurrence of inflammatory carcinoma; this type of case always extends rapidly.

rences must be set apart from those cases in which a reasonable palliation, if not a considerable regression of the disease, may be expected. All that one may hope to accomplish for those patients with a far-advanced lesion is a relief of their suffering by adequate amounts of codein or morphin; frequent dressings, when foul ulcers are present, are perhaps at times sufficient to satisfy the mind of the patient that treatment is still in progress. If we therefore exclude these patients from the whole number, 218 cases, we have remaining 124 patients in whom irradiation as a therapeutic agent could be entertained with a fair hope of some favorable result.

THE PREVENTION OF RECURRENCE

Proper Selection of Cases. In the recent rapid development of therapy by roentgen ray and radium the surgeon has at times seemed unwilling to relinquish anything in the surgical treatment of cancerous disease. The presence of a carcinoma in a breast is not necessarily an indication for a radical amputation, for a careful physical examination of the patient may reveal some factors which would militate against success by operation. The cases treated surgically

FIG. 27. Diffuse cutaneous metastases before irradiation.

must therefore be well chosen if the percentage of recurrence is to be kept at a minimum.

Preoperative Irradiation. It has been the practice at the Memorial Hospital for several years to give a preoperative cycle of roentgen rays in every case of carcinoma of the breast before submitting the patient to operation. As a rule, a period of from seven to ten days is allowed to elapse between the time of the last irradiation and the day of operation. We believe that the preoperative cycle is of great service in forestalling recurrence, but up to the present time a sufficient number of cases has not been accumulated to furnish a

proper comparison with groups of patients in other clinics where the preoperative use of the roentgen ray has been omitted; eventually such a study will unquestionably furnish a proper estimate of the real value of preoperative treatment. In the vast majority of cases we have seen no evidence which would lead us to believe that the preoperative cycle interferes materially with wound healing, or adds to the liability of wound infection.

Postoperative Irradiation. From two to three weeks following operation, every patient is subjected to a post-

Fig. 28. Disappearance of cutaneous metastases following irradiation (same case as in Fig. 27).

operative series of roentgen-ray treatments over the whole breast and drainage areas. An interyal of from six weeks to two months is then allowed to elapse, when a second similar cycle is administered. Sufficient data have already been accumulated at the hospital to make one feel very certain that postoperative treatment prevents certain recurrences and postpones the appearance of practically all recurrences. In addition, it unquestionably prolongs the life of the patient. We feel, therefore, without any reservation, that postoperative irradiation has proved its worth.

RESULTS OF TREATMENT

One may well ask what the average expectation of life is from the time of the first appearance of a recurrent breast tumor without any irradiation. Such a question might imply that all breast cancers are of the same pathologic type and follow a similar clinical course. We know that this is not the case. At present, with the cooperation of Dr. James Ewing,

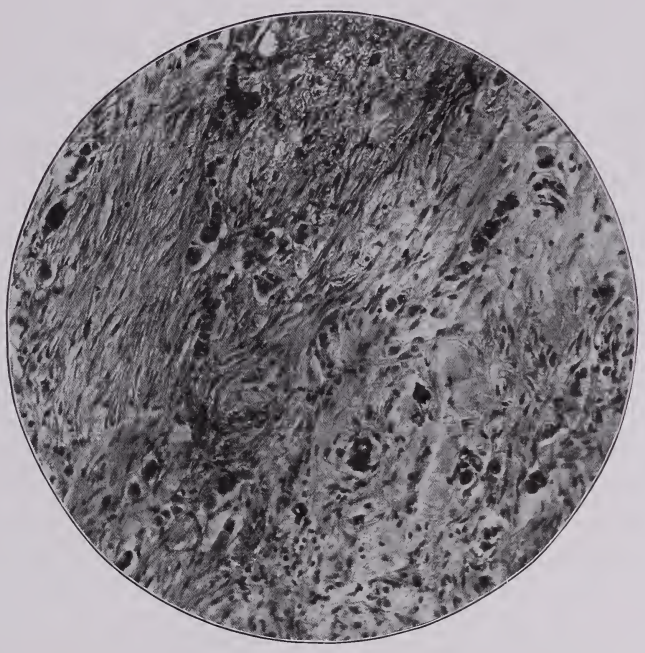


FIG. 29. Granular degeneration of cell bodies; hyperchromatism of nuclei, and granular degeneration of the stroma.

pathologist at the Memorial Hospital, we are engaged in an effort to classify more satisfactorily the various types of carcinoma from a pathologic point of view and to study their reaction to various forms of irradiation. A papillary adenocarcinoma, a tumor well known to be of low-grade malignancy, will certainly permit a longer period of life following recurrence than a rapidly growing cellular tumor. Similarly a fibrocarcinoma in a woman of seventy may be expected to grow with much less rapidity following reappear-

ance of the disease than a fulminating recurrence complicating pregnancy in a young woman. Nevertheless a gross clinical judgment as to the value of irradiation as a means of treatment for recurrence may be reached if we compare results giving the duration of life from the appearance of recurrence in nonirradiated and irradiated patients.

At the New York Hospital, in the First Surgical Division, where, through the courtesy of Dr. Charles L. Gibson, I was able to follow the breast cases especially, the length of life after recurrence in a series of 22 patients on whom a radical amputation had been performed with no subsequent irradiation, was six and a half months. In the patients in the present series, who have been treated by irradiation following the appearance of recurrence, the length of life after recurrence has been two years and four months, a decided advantage, as one may readily see, in favor of irradiation.

Of the total of the 124 patients in whom some favorable results from irradiation might be expected, 31 are alive at the writing of this report, which is 25 per cent of the total number. Of the 31 patients, 22 are doing well, while 9 are doing badly. A brief table is given, that the data may be more readily available.

In general, the more cellular the tumor, the better the response to treatment by irradiation. The younger the woman and the more rapid the recurrence, the poorer is the result to be expected from irradiation.

TYPES BEST SUITED FOR IRRADIATION BY RADIUM

Small localized lesions in the infraclavicular region, or adherent to or involving the chest wall, small localized skin metastases or small accessible nodes are most amenable to treatment by radium itself.

Some of our best results following the use of radium in the recurrent group have been in the infraclavicular region. In some of these cases, applications of a radium pack have resulted in a complete disappearance of the growth. One of the patients has now gone one and a half years with no further evidence of disease to be made out. The details of radium therapy and the methods employed

RESULTS IN THIRTY-ONE CASES

Case	Operation to recurrence		Recurrence to date		Total duration after operation	
	Years	Months	Years	Months	Years	Months
Patients doing well						
1	..	6	3	8	4	2
2	13	..	6	..	19	
3	..	7	4	10	5	5
4	..	3	6	4	6	7
5	..	3	4	8	4	11
6	..	2	3	..	5	
7	2	3	3	5	5	8
8	..	1	2	9	2	10
9	..	..	3	2	3	2
10	2	..	2	10	4	10
11	..	3	1	8	1	11
12	..	..	2	..	2	
13	..	1	2	2	2	3
14	1	..	1	6	2	6
15	..	9	1	7	2	4
16	7	1	2	4	9	5
17	2	..	1	8	1	10
18	1	1	2	2	3	3
19	1	7	1	11	3	8
20	8	..	1	10	2	6
21	6	4	2	2	8	6
22	10	..	1	10	2	4
Patients doing badly						
23	..	3	5	..	5	3
24	1	1	3	..	4	6
25	1	..	3	8	4	8
26	..	..	2	10	2	10
27	..	11	4	9	5	8
28	1	6	3	6	5	
29	..	6	2	3	2	9
30	4	..	2	7	6	7
31	3	..	2	3	5	3

have been fully described in a recent article,[1] and will not be recounted here.

TYPES BEST TREATED BY THE ROENTGEN RAY

Recurrences best treated by the roentgen ray include diffuse cutaneous involvement, examples of so-called inflammatory carcinoma, extensive involvement of nodes in the axillary or supraclavicular regions, and mediastinal or pleural metastases, as well as bony metastases, in various parts of the body. The technique employed has been fully described in a recent paper. At present we are still depending mainly on the old type of roentgen-ray machine, and have been reasonably satisfied with the results obtained. Some of the most striking effects have been seen in the treatment of diffuse cutaneous involvement, an area of considerable disease disappearing in a few weeks under appropriate irradiation, leaving an apparently normal skin. In some of these cases a later follow-up has shown a reappearance of the iesion.

The new 200,000-volt machine now in operation is being used on carefully chosen patients, but sufficient time has not elapsed to make any report on this method of therapy. We are very hopeful that some of the mediastinal and pleural extensions of the disease may yield encouraging results through this new method of treatment.

The gross and microscopic effects of the treatment of cancerous diseases by radium and the roentgen ray will not be enumerated here, as they have been described elsewhere.

CONCLUSIONS

1. As a prophylaxis against the recurrence of breast carcinoma, a careful selection of patients for operation must be made.

2. Preoperative and postoperative cycles of roentgen rays are important prophylactic measures against recurrence.

3. A follow-up in every patient with carcinoma of the breast operated upon should be adopted as routine. No surgeon should operate on a patient with breast cancer

[1] Lee, B. J. Results to date in the treatment of primary inoperable carcinoma of the breast by radiation. *Ann. Surg.*, Sept., 1922.

without appreciating that an integral part of the procedure is following up the patient, with the idea in view of discovering the appearance of metastases at an early date, permitting the application of irradiation as soon as possible.

4. Properly applied irradiation to recurrent breast carcinoma definitely prolongs the life of the patient.

5. I believe that ultimately, with more complete knowledge and better technique, a still further control of the recurrent phase of this disease may be expected.

XIII

RESULTS OF THE TREATMENT BY RADIATION OF PRIMARY INOPERABLE CARCINOMA OF THE BREAST[1]

Burton J. Lee, m.d.

Since the establishment of the breast clinic at Memorial Hospital in the fall of 1919, there has been a systematic effort to study the whole problem of carcinoma of the breast. Beginning with the pioneer work done by the late Dr. H. H. Janeway, prior to 1919, considerable progress has been made in the treatment of inoperable mammary cancer by radiation, and the present report includes not only the cases under my own supervision, but also those of my colleagues at the hospital. All the patients were admitted in the years 1918, 1919 and 1920, leaving a period of sixteen months since the last case under report began treatment.

A primary inoperable breast carcinoma is one in which one or more of the following factors are present:

A. Fixation of the breast tumor itself to the chest wall.

B. Involvement of the supraclavicular nodes.

C. Definite involvement of the opposite axillary nodes.

D. Diffuse subcutaneous nodules.

E. Diffuse inflammatory carcinoma involving a considerable skin area.

F. Chest metastases—pleural or mediastinal.

G. More remote metastases.

All surgeons will not perhaps be in accord with these indications of inoperability.

A. We believe that fixity to the chest-wall places the patient in the inoperable class. Under these circumstances several additional areas are usually the seat of the disease.

[1] Read before the American Surgical Association, May 1, 1922. Reprinted from *Ann. Surg.*, Sept., 1922, lxxvi, No. 3, pp. 359–385.

B. We have considered involvement of the supraclavicular nodes a sign of inoperability because we believe that a complete dissection of this area is practically impossible without a division of the clavicle itself. We have taken this position after careful consideration of the usual course of the cases with supraclavicular involvement, with and without operation.

In the clinic, several cases which we had considered inoperable because of supraclavicular involvement, and were treating by radiation, have gone elsewhere and had a radical operation performed. One such case entered the clinic with definite, small, hard supraclavicular nodes. She returned six weeks later following a radical amputation, with the supraclavicular nodes three times as large as when we first saw her, and in spite of any type of radiation, is rapidly succumbing to the disease. In our judgment, this patient was made distinctly worse by the radical procedure adopted. We have also noted that a definite fulness in this region often precedes the appearance of distinct nodes, the first node usually palpable being the one directly behind the inner end of the clavicle. Nevertheless, this sequence is not invariable, and we consider the case inoperable only when definite, firm nodes may be palpated.

C. If the surgeon cannot palpate axillary nodes, it is no proof that numerous small nodes may not be present; but when a definite hard node is to be felt in the opposite axilla, one may feel reasonably sure that this indicates carcinomatous involvement. Not infrequently we have found the opposite axilla the seat of disease, often without apparent involvement of the opposite breast.

D, E. No question can exist in the mind of any surgeon, that the patient is inoperable in the presence of diffuse subcutaneous nodules, or diffuse cancerous involvement of the skin. We have numerous examples of these types of metastases in the clinic, treated by operation or radiation, or by both methods, and we have a very deep conviction that radiation offers much the better outlook for the patient.

F, G. No one can doubt that pleural and mediastinal metastases, as well as a spread of the disease to remote areas, indicates inoperability.

A case having been classified, two questions are asked concerning it:

I. What can be done for the primary inoperable carcinoma of the breast?

1. Check considerably the rate of growth of the carcinoma, frequently causing a considerable regression and at times a disappearance of the carcinoma. The persistence of a mass in the breast may not necessarily indicate that active carcinoma is still present. Fibrous tissue replacement may leave a definite hard tumor mass, which may be misleading in estimating the exact effect of radiation upon the tumor itself.

2. Involved nodes in the axillary or supraclavicular regions may be expected to regress considerably, and in some instances they have entirely disappeared under treatment by radiation.

3. A fixed breast tumor may be rendered mobile, permitting a palliative operation with removal of the breast itself, eliminating the possibility of subsequent ulceration. Four of our patients who are doing particularly well received this type of treatment.

4. Relieve in some measure the patient's discomfort and pain. The effect upon spinal metastases has been variable, but in a few instances there has been a marked relief of pain over a considerable period.

One is compelled to admit that certain cases presenting themselves at the hospital are altogether too advanced to hope for any good result by any means of treatment. Too much emphasis cannot be placed upon the unwisdom of promising patients with advanced disease remarkable results from radiation or any other form of treatment. Such cases, however, are often given mild *x*-ray radiation for the moral effect, but the family are told what we believe to be the truth concerning the case. The Social Service Department of the hospital has done a fine humanitarian work in the care of these patients—dressing ulcerating areas where home conditions of the patients permit it, and providing for the entry of other cases into institutions devoted to this incurable group.

But the surgeon may ask at once: "Is not this a general disease? And what of the mediastinal, pleural and pulmonary metastases, as well as those of the spine, liver, etc.?" We fully appreciate the rapidity with which dissemination occurs and are convinced that it spreads far more rapidly to other areas than we have fully realized. Nevertheless, at first it is a local disease and therefore amenable to local attack in its early stages. I venture to express the belief that ultimately a more complete radiation of the chest areas will be routinely practiced in the effort to forestall and check any possible early involvement in these regions. The problem of such a program is not devoid of many practical difficulties, for normal intervening tissues are also extensively radiated and the patient's general resistance may be seriously lowered with marked anemia and aggravated digestive disturbances following a prolonged radiation; therefore any effort completely to radiate the chest and mediastinum must take into account the patient's general strength and her reaction to radiotherapy.

II. What may we learn from the patient?

The clinical pathological data being developed in the institution will ultimately throw much light upon this problem. Statistics are always uninteresting and frequently misleading, but there are a few facts concerning the group under report which I will briefly touch upon:

Age. The age of the patients varied from twenty-two to eighty-four years, the average being fifty-four.

Between the ages of twenty-one and thirty	2 patients
Between the ages of thirty-one and forty	11 patients
Between the ages of forty-one and fifty	22 patients
Between the ages of fifty-one and sixty	28 patients
Between the ages of sixty-one and seventy	11 patients
Between the ages of seventy-one and eighty-four	7 patients

(In two patients, no age was mentioned.)

Trauma. As a possible etiological factor, fairly definite trauma was present in 24 of the 83 cases, or 28.9 per cent.

Lactation. Thirty-five of the patients had never had a lactating breast, a percentage of 42.2 per cent. Approxi-

mately one-third of the patients presenting themselves at the hospital with breast carcinoma have never had a lactating breast.

Pathology. Whenever it is possible, a section of the tumor tissue is secured. We are succeeding more regularly in this effort in the past two years than in the years 1918 and 1919, there being pathological reports upon 34 of the 83 patients, six upon very advanced cases and twenty-six out of the 57 patients considered suitable for treatment. Of the 33 cases in which pathological examinations were made, 8 showed fibrocarcinoma, 12 carcinoma simplex, 9 alveolar carcinoma, 4 infiltrating carcinoma, and 1 plexiform carcinoma. In 5 instances the tumor was believed to have a sweat-gland origin rather than one from breast tissue itself. We hope later to develop some data upon the behavior of these so-called sweat-gland carcinomas of the breast.

The primary inoperable carcinoma has usually gone into the infiltrating stage, whatever the primary type of tumor may have been. In fact, if one searches diligently throughout the whole tumor one may find varied types of carcinoma, perhaps in one section fibrocarcinomatous elements and in another area a more markedly cellular appearance. Early in the disease certain anatomical types may be expected to run a certain clinical course. An encapsulated adenocarcinoma, which later goes on to a fungating stage, runs an entirely different clinical course from that of a hard fibrocarcinoma of an older woman or a diffuse, markedly cellular carcinoma in a young woman. However, when the disease has become more fully developed, a histological study of a single specimen removed from a breast cancer may give very little information to the surgeon concerning the probable clinical course of the disease from that time on. Nevertheless, it is advantageous that pathological data be obtained whenever it is possible.

Treatment by Radiation. Frequent visits to the breast follow-up clinics make it possible to obtain accurate data upon the progress or regression of the disease. A weight record gives a very fair index of the patient's state of health, though we have observed in many instances an advance of the malignant process with no loss of weight or obvious

impairment of the health. Upon the other hand, when a patient with inoperable breast cancer begins to lose weight rapidly, we realize that not many months will elapse before the patient will succumb to the disease. In his study of the treatment of breast carcinoma by radiation, the writer wishes gratefully to acknowledge the hearty cooperation given to him by Dr. Herendeen, the roentgenologist at the Memorial Hospital.

Treatment by X-rays. If the growth is one of considerable size, we usually rely upon *x*-ray radiation. This is given in cycles of four or five treatments per cycle, at intervals of one, two or three days between treatments. The breast, anterior chest-wall, lateral chest-wall, axillary and supraclavicular regions are covered by this radiation. The usual dosage with a 10-in. spark-gap is fifteen minutes of treatment, using a 10-in. focal distance, 4 ma. of current, and 4 mm. of aluminum filtration. This gives the average patient a very definite erythema of the skin, but no blistering. There is, however, a wide variation in susceptibility to radiation, and, while some stand a larger amount of radiation than others without damage to the skin, in general the dosage outlined is a safe one to use. The danger of overradiation by *x*-rays must always be borne in mind. It is far better to be satisfied with a reasonable result than to attempt the impossible. Marked telangiectases developing in the skin should be considered a contraindication to further treatment by radiation. If this precaution is not observed ulceration will often ensue with, at times, a development of an epithelioma. There is no instance in this report of any patient developing epithelioma from overradiation.

If the tumor tissue is quite superficial, or there are numerous subcutaneous nodules, or there is a diffuse pesudo-inflammatory involvement of the skin by the new growth, *x*-ray treatment for a short period, giving a superficial dosage, yields the best results. There have been some remarkable disappearances of skin nodules and carcinomatous skin involvement by this means. As a rule the whole side is radiated, including the supraclavicular and axillary regions. An interval of five or six weeks is allowed to elapse before the second cycle of treatment is undertaken, and in

the meantime the patient is seen several times, that the reaction to radiation may be observed.

As a rule, the effect upon the breast tumor or upon axillary or supraclavicular nodes from this type of radiation is a distinct diminution in size appreciable in from three to seven weeks. If after two or three such cycles there seems to be no further advance in the disease, it is wiser to defer radiation for a period, the patient meanwhile being kept under observation.

We are convinced that unless the radiation causes a considerable erythema of the skin, the underlying mass does not receive sufficient radiation to affect properly the carcinomatous cells. Systematic treatment of chest metastases has not yet been undertaken at the hospital, but we are hoping that something may be accomplished with our new high-powered machine now in operation, giving 200,000 peak voltage through the tube with a spark-gap of 14 in. One cannot, however, forget, when radiating carcinoma deep within the chest cavity, that everything between that point and the source of radiation is also being heavily radiated, furnishing a serious obstacle to effective radiation of the tumor.

Treatment by Radium. Those cases best suited to radiation by means of radium are small breast tumors with involvement of axillary and supraclavicular nodes, and tumors involving the sternum and chest-wall to a moderate degree. With the small breast tumor, after complete *x*-ray radiation, the insertion of radium bare tubes, using 1 mc. per c.c. of breast tumor, gives very satisfactory results. This insertion of bare tubes is done under novocaine anesthesia. The tubes are introduced through needle cannulæ, the little glass tube containing the radium emanation being forced into the breast tumor at any desired point by pressing a minute plunger in the needle. This must be done in a very systematic fashion, and one must be reasonably certain that all parts of the tumor have received an adequate insertion of radium. The same method may be employed in the axillary region if the nodes are not closely adjacent to the brachial plexus or not too deeply placed in an inaccessible position. One may introduce these tubes to within a distance

of 1 cm. from the nerves; but closer introduction will cause an intractable case of neuritis. The bare tubes containing the radium introduced through the skin or through a minute incision, which also permits the removal of a section, must never be placed nearer than 1 cm. from the outer surface of the skin, or ulceration will ensue. The treatment by bare tubes has given us some excellent results, with complete disappearance of the tissues in some instances, over a period of two years up to the present writing.

Upon the other hand, a case which has received extensive external radiation by *x*-ray or radium, with beginning areas of telangiectasis, is a poor one in which to insert radium bare tubes, as the tissue vitality is poor and ulceration may ensue. In a tumor a little larger, say 4 cm. in diameter and upwards, we frequently make use of a platinum needle carrying 50 to 70 mc. of radium gas, contained in glass tubes, the platinum needle having a thickness of 0.4 mm. This is introduced through the skin into the tumor and is allowed to remain there until the new growth receives approximately 50 mc. hrs. of treatment for each cubic centimeter of tumor tissue. The needle is partially withdrawn at fixed intervals, permitting radiation of additional parts of the tumor. We have had some excellent regressions by this method, and in one instance an entire disappearance of the tumor. A sufficient time, however, has not elapsed to determine whether or not there may be a reappearance of the carcinomatous mass.

External radiation by means of a radium pack, using 8500 to 9000 mc. hours for 70 sq. cm. of surface, at a distance of 6 c.c. from the skin, with a filtration of ½ mm. of silver and 2 mm. of brass, gives frequently an excellent regression in a small, well-localized tumor of the breast, sternum, or chest-wall; and axillary nodes are also treated by a similar pack placed over the base and anterior aspect of the axilla. The supraclavicular region is best radiated by means of the brass tray containing radium emanation, if the nodes are superficial, the distance from the skin being 3 cm. with a filtration similar to that of the pack, giving 2500 to 3000 mc. hrs. of treatment. If the nodes are extensively involved or more deeply placed, the pack is preferable. External radiation

with radium may be repeated at the same interval used with *x*-ray treatments, and patients are followed in the meantime to determine the exact response to radiation.

Pathological Changes due to Radiation. Aside from the clinical evidence of marked diminution in size or even complete disappearance of a tumor by radiation, there are also macroscopical and microscopical changes. Macroscopically small areas of necrosis may be seen for a distance of 1 cm. in all directions from the point of insertion of radium bare tubes, and the small type of gross necrosis may be evidenced following external radiation. The microscopical effects following treatment by radium and *x*-rays may be very marked, consisting of hyperchromatism of the nuclei, hydropic degeneration of the cytoplasm of the cell, and a granular degeneration of the connective-tissue stroma surrounding the carcinomatous cells. Ultimately the tumor cells may disappear and nothing but a granular detritus remain. Frequently, well-marked endarteritis may be observed in the blood-vessels within the radiated area. Eventually the fully radiated areas are reduced to hard fibrous cicatricial tissue.

Duration of Life. We have found such startling differences in the life-histories of these cases that at times it almost seems as if the rapid and the slow cases must be different diseases. One patient presenting herself at the clinic had never been operated upon and had never been treated, but had lived for twenty-two years with a carcinoma *en cuirasse* covering a large part of the anterior chest-wall. She eventually succumbed to the disease. At the moment we doubt the wisdom of attempting to draw any conclusion as to the prolongation of life in a case of inoperable carcinoma of the breast treated by radiation. Few figures upon this subject can be obtained. Lazarus Barlow stated as far back as 1904 and 1905 that the average life of untreated carcinoma or unoperated carcinoma of the breast was thirty-eight and a half months.

The total duration of life of patients in this report is as follows:

In the very advanced group (of 26) we found that the duration before treatment averaged two years, five and eight-

tenths months, with a maximum duration for one patient of twenty-two years, and a minimum duration of two weeks. The duration after admission to the hospital averaged approximately four months, with a maximum duration of one year, and a minimum duration of two weeks. The average total duration of life for the very advanced cases was two years, nine and two-tenths months. Maximum duration: twenty-two years, five months; minimum, nine weeks.

I. *Doing badly*

No.	*Initial*	*Duration after Treatment*
5	E. M.	3 years, 8 months
8	A. T.	3 years, 5 months
18	A. H.	2 years, 9 months
23	M. K.	3 years
29	M. B.	15 months (data incomplete)
28	A. B.	1 year, 6 months
31	C. D.	2 years, 3 months
41	C. M.	13 months (data incomplete)
43	M. M.	2 years, 2 months
48	M. O.	1 year, 7 months
51	A. H.	15 months (data incomplete)
55	L. G.	1 year (data incomplete)

II. *Doing well*

No.	*Initial*	*Duration after Treatment*
9	L. N.	4 years
25	A. S.	2 years, 9 months
26	E. T.	3 years, 5 months
30	M. C.	1 year, 7 months
32	M. D.	1 year, 6 months
33	E. A.	1 year, 5 months
35	T. C.	1 year, 5 months
36	A. F.	1 year, 11 months
44	S. M.	1 year, 10 months
46	M. M.	1 year, 10 months
47	M. N.	2 years, 5 months
53	A. R.	2 years, 1 month
56	M. S.	1 year, 8 months

In cases that seemed suitable for treatment we found that the average duration before treatment was two years, four months, the longest duration in one case being eighteen years, the shortest one month. The duration of life after admission gave an average of one year, seven and a half months, the longest duration being four years, and the shortest two months. The average total duration of life in these 57 cases was four years and three-tenths of one month, the longest case giving a duration of nineteen years and eight months, and the shortest, one year, two months. As one may readily see, the average duration in the 57 cases favorable for treatment was almost a year longer than the figure of thirty-eight and a half months quoted from Barlow.

Finally, as to the living and the dead. At the present writing all of the 26 advanced cases are dead. Of the 57 cases which seemed worthy of treatment, 25 are to-day alive and 13 of them are doing well.

The average duration of life after treatment of those doing well is two years, three and one-tenth months, the longest duration since treatment being four years, the shortest one year and five months.

CONCLUSIONS

In conclusion the following points should be emphasized:

1. Primary inoperable carcinoma of the breast has shown good results by radiation.
2. The patient must be kept under constant clinical observation.
3. The type of radiation must be properly selected for each individual case. No routine prescription will suffice.
4. Overtreatment by radiation must be avoided.
5. Very advanced cases are unsuitable for any form of treatment.
6. The palliative operation following properly planned radiation is of service in well-selected cases.
7. A cooperating Social Service Department makes a follow-up system effective and gives humanitarian relief to hopeless cases.

8. The results to date are very gratifying and encouraging. We believe that as the disease itself and the technique of radiation become better understood, more and more satisfactory results will follow, and that the possibility of still further control of the disease by radiation may ultimately be realized.

XIV

CARCINOMA OF THE PROSTATE[1]

BENJAMIN S. BARRINGER, M.D., F.A.C.S.

Carcinoma of the prostate presents as many complexities of diagnosis and treatment as any other disease of the urological tract. The internal situation of the prostate, the confusion between carcinoma and adenoma, the quiet, often symptomless, invasion of the prostate by the carcinoma, the urinary retention, the conflict between operative and radium treatment—these are some of the phases. In this paper only the most important problems of diagnosis and treatment are considered. It is especially an attempt to bring up to date the report of radium therapy in carcinoma of the prostate as practiced at the Memorial Hospital.

GROSS PATHOLOGY—TYPES OF CARCINOMA

The two following histories with their post-mortem data represent two types of carcinoma between which extremes all variations occur.

CASE 1. Male, aged sixty. Admitted to Memorial Hospital, September 11, 1919, with a history of frequency of urination and prostatic retention for a number of years.

The examination of his prostate (by rectum) revealed a very large, irregular, stony, hard prostate fixed to the pelvis. Indurated masses extended along the right and left vesicles. The top of these masses could not be felt. The patient was very thin and cachectic. Residual urine 4½ oz. Radium had no effect that could be determined by palpation upon the carcinoma. Patient gradually grew worse and died December 3, 1919. The post-mortem record showed: Kidneys—ascending suppurative pyelonephritis; prostate—measures 4 by 5 cm. laterally and 2½ cm. vertically. Structures are obliterated by opaque tumor tissue which fungates, through base of bladder at trigone, 3 cm. wide.

[1] Reprinted from *Surg., Gynec. & Obst.*, Feb., 1922, No. 2, xxxiv, 168–176.

Rectal wall is slightly adherent but not involved. Peritoneal surface behind bladder base shows superficial subserous nodules. *No enlarged lymph-nodes were found.* The carcinoma was not extended above the seminal vesicles.

Case 2. Male, aged seventy-four. Admitted to Memorial Hospital, August 24, 1916. His chief complaint was a tumor mass on left jaw. Seven months previously he had had a severe facial neuralgia, and then a small lump appeared on the left cheek anterior to ear. The lump increased in size. Patient lost strength and weight rapidly, 34 lbs. in a "short time." Lately he has had some "stomach trouble." The physical examination showed: No teeth in either jaw; above left molar region of inferior alveolar process is a small area of tumor of the size of a 5-cent piece. Extending into adjoining buccal mucous membrane is a hard tumor growth which involves the whole side of the inferior maxilla producing a large tumor of the left cheek. The tumor is hard and fixed to the inferior maxilla. Rectal examination showed the prostate slightly enlarged and very irregular. The left lobe was larger than the right. Small, hard nodules appear on surface, but there is no perivesical enlargement. Diagnosis: *probably primary prostatic carcinoma* with metastases to jaw.

The post-mortem showed: Kidneys, left pyelitis and chronic productive nephritis; right pyelitis. The bladder showed chronic suppurative cystitis. The left lobe of prostate was slightly enlarged and showed pea-sized nodules projecting from the posterior surface. At entrance to prostatic urethra surrounding orifice were a few soft, pea-sized papillary projections. Running up the spinal column was a series of slightly enlarged lymph-nodes becoming more marked in the thorax, and replaced by soft tumor tissue. In the thorax, the process from lymph-node invaded the body of the fourth and fifth dorsal vertebræ. This process encircles the spine and invades the periosteum of the sixth and seventh ribs, largely destroying both. The entire left inferior maxilla is destroyed by a soft tumor process, which invades the periosteum and replaces bone. Diagnosis: carcinoma of prostate; secondary carcinoma of inferior maxilla by invasion through spinal lymph-nodes.

In the first case (of low malignancy) notwithstanding the time the disease had been present and the very large prostatic carcinoma, the carcinoma did not go above the seminal vesicles. In the second case (highly malignant) the changes in the prostate were so slight as to make the diagnosis of carcinoma only "probable," yet the metastases were very large and extensive.

Both of these extreme types are rare and all gradations between them are seen. The usual type is a slowly growing tumor which, because of the limiting fascia of Denonvilliers on the one side and the bladder base on the other, generally grows in the line of least resistance, upward into the lymphatics around the seminal vesicles, and metastasizes very early in its life history.

FREQUENCY OF GROWTH BEYOND THE PROSTATE IN 145 CASES

In 2 cases the carcinoma, as far as could be determined by palpation, was confined to the prostate; a third case was borderline. The remaining 142 cases showed extension either toward the vesicles to the bladder, to the lateral walls of the pelvis, or metastases to more distant parts of the body.

Lateral Pelvic Extension. The most common extension of a prostatic carcinoma is toward the seminal vesicles. A second not uncommon extension may be to the lateral pelvic walls. From either prostatovesicular junction, a bridge of dense carcinomatous tissue is felt extending to each ramus of the pubes. This is a common extension and one not usually described.

Recial Extension. There were but 3 cases of growth of the carcinomas through the rectal wall at the site of the

FIG. 30. Punch used for suprapubic removal of carcinomatous prostatic base.

prostate. This growth was accompanied by vesicorectal or urethrorectal fistulæ and was not to be confused with the perirectal growth often occurring above the seminal vesicles and causing rectal stricture.

Anterior Urethral Metastases. One of the 145 cases had metastasis in the anterior urethra. This was either a retrograde lymphatic growth or a direct implant into the urethral mucous membrane. In this case metastasis occurred after a Young punch operation on the bladder neck. Carcinomatous tissue broken loose might have formed a transplant. This patient also had a secondary nodule of the head of the penis.

I have seen one other case which had a periurethral metastasis some centimeters back of the head of the penis. In this case there had been no operation on the prostate or urethra.

Distant Metastasis. Our records are too imperfect to determine how frequently prostatic carcinoma metastasizes to the pelvis, lumbar spine, lungs, long bones, glands, etc. Bumpus[1] has lately published records on the frequency of these metastases.

Prostatic Carcinoma Secondary to Bladder Carcinoma

A bladder carcinoma usually starts in the mucous membrane of the bladder, and grows in the line of least resistance, that is, into the cavity of the bladder. Nothing hinders its growth in this direction. So having ample space within which to grow, it metastasizes late. When the bladder con-

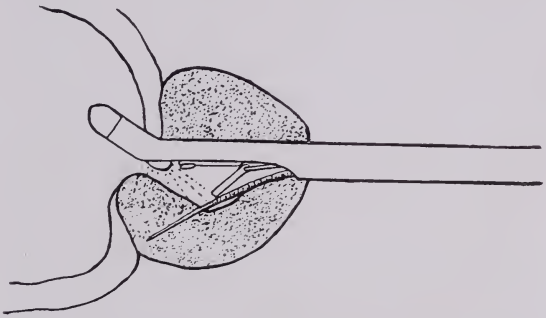


FIG. 31. Method of inserting bare tubes of radium into carcinomatous prostatic base to relieve residual urine.

tracts to expel urine, the mucous membrane folds up and there is not much pressure exerted upon the tumor. A prostatic carcinoma, on the other hand, has no space in which to grow. In addition to this it is limited posteriorly by the dense fascia of Denonvillier and anteriorly by the less dense fascia of the bladder base. This tension, so to speak, in which the prostatic carcinoma is held, is one factor in causing it to extend beyond the prostate and metastasize early, and it metastasizes or extends most often upward between these two limiting fasciæ. Probably a contributing factor to early metastasis is the pressure exerted upon the carcinoma when the bladder sphincter contracts at the end of each act of

[1] BUMPUS, H. C. Carcinoma of the prostate. *Surg., Gynec. & Obst.*, July, 1921, No. 1, xxxii, 31.

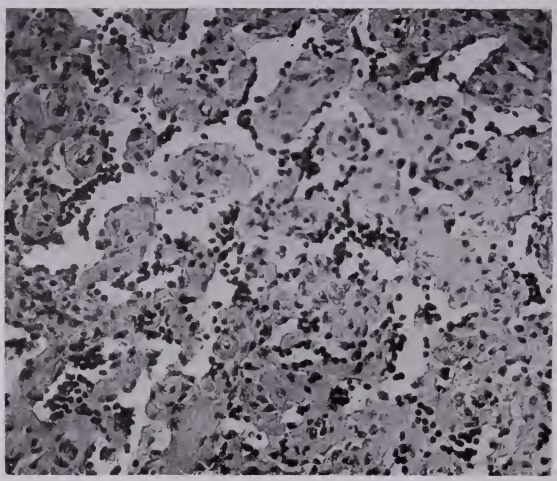


FIG. 32. Radium changes in epidermoid carcinoma of bladder. Carcinomatous cell groups breaking up.

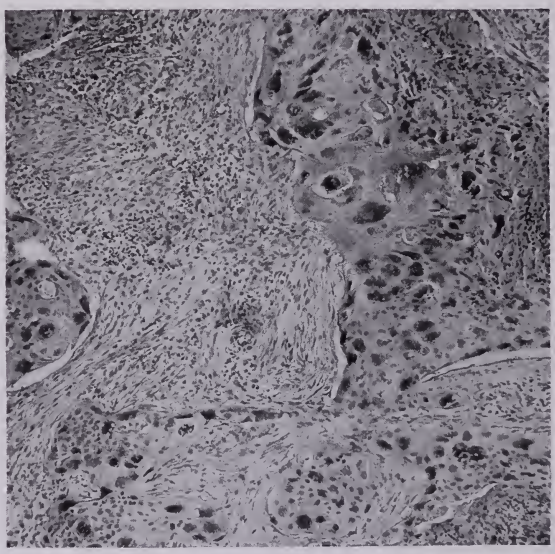


FIG. 33. Epidermoid carcinoma of bladder growing into prostate and clinically giving picture of prostatic carcinoma.

urination. Because of these conditions it is rare for a bladder carcinoma to grow by the difficult route and invade the prostate, but rather common for a prostatic carcinoma to break through the fascia at the bladder base and invade the bladder. The following case is the only one of the series in which the picture was that of prostatic carcinoma, but the pathological report showed a squamous-celled carcinoma undoubtedly originating in the bladder.

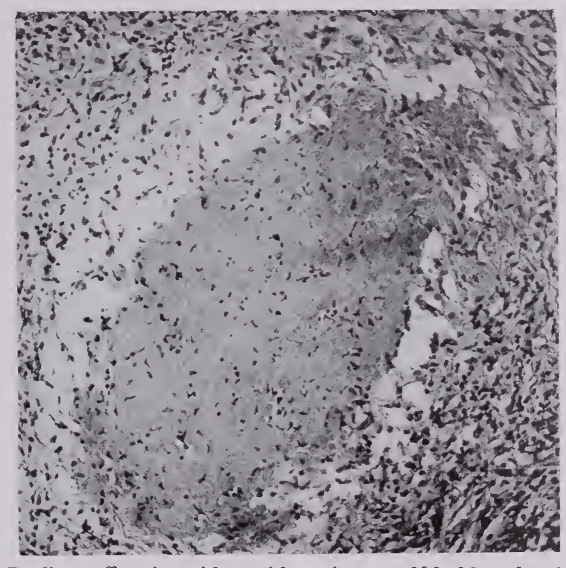


FIG. 34. Radium effect in epidermoid carcinoma of bladder, showing necrosis.

Male, aged sixty. First seen July 5, 1920. In October, 1919, he suffered with frequency of urination. February, 1920, he became impotent. He never had hematuria.

The prostate shows a hard tumor mass of the posterior lobe of the prostate 2½ by 3 cm., stony, hard, fixed and irregular, and one cannot feel above the prostate to determine the condition of the vesicles. He has complete retention of urine.

In December, 1920, a suprapubic prostatomy was done to relieve retention of urine. All around the internal urethral orifice were irregular carcinomatous nodes, very extensive, forming valleys and hills. The whole bladder base was indurated, a typical picture of a prostatic carcinoma growing into and behind the bladder wall. The patient died, uremic, in January, 1920. The pathological report (Dr. Ewing) follows:

"The tumor has the structure of an epidermoid carcinoma, the cells being broad, flat and mostly of distinctly squamous character. It shows none of the

glandular features of prostatic carcinoma, and it appears quite improbable that it has any other origin than from the bladder mucosa.

"The radium changes are notable. The first changes consist of extreme swelling and hyperchromatism, often followed by disintegration of the nuclei. Many of these cells form giant masses. Hydropic swelling is also present. Later the cell groups break up, and become very hydropic, while the surrounding connective tissue reacts with production of much cellular granulation tissue. Finally the tumor cells disappear, often leaving giant cells or points of necrosis, much resembling miliary tubercles."

EARLY SYMPTOMS

1. *Disturbance of Urination.* Of 145 cases, 115 had as a first symptom either dribbling, dysuria, nocturia, frequency, difficult urination, or retention, or a combination of these; 11 had, as a second or subsequent symptom, some disturbance of urination.

2. *Hematuria.* Eight had hematuria as a first symptom, and 25 as a second or subsequent symptom. Of 33 cases which had hematuria as a symptom it is definitely stated that the bladder had a secondary carcinoma in 18.

3. *Pain* (not associated with urination). Seven had pain as a first symptom—3 in back, 1 in back and hip, 1 in heel, 1 in prostate, 1 in abdomen; 5 had pain as a second symptom. One had pain in groin, 1 in buttocks, 1 sciatic, 1 in thigh, 1 in leg.

One patient had as a first symptom edema of legs; 1, a swollen testicle; 1, constipation; 1, bleeding from rectum.

There is nothing in the symptoms that can distinguish carcinoma from nonmalignant enlargement of the prostate, although in the latter a history of hematuria is somewhat more frequent.

AGE—129 CASES

30 to 40 years	2
40 to 50 years	5
50 to 60 years	33
60 to 70 years	59
70 to 80 years	27
80 to 90 years	3

Here again the age incidence runs nearly parallel to that of hypertrophy of the prostate.

Time Elapsed between Time First Seen and the First Appearance of Symptoms

In 93 cases of prostatic carcinoma with the growth extending beyond the prostate, the time elapsing between time first seen and the first appearance of symptoms is:

1 to 2 months	15
2 to 4 months	12
4 to 6 months	11
6 to 12 months	19
12 to 18 months	7
18 to 24 months	8
24 to 36 months	7
36 to 48 months	4
48 to 60 months	6
60 to 72 months	3
72 plus months	1

One unusual case was that of a patient with extensive carcinoma of the prostate who had had a prostatectomy for prostatic carcinoma nine years before.

The hopelessness of curing many cases of carcinoma of the prostate if we do not radically change our method of approach is shown by these figures. Notwithstanding that 1 out of 7 cases came within the first two months after the appearance of symptoms, that 1 out of 3 cases came to us within six months, and 2 out of 3 within the first year of symptoms, in all these cases the carcinoma had grown beyond the prostate. *We are inevitably forced into the conclusion that regular examination of the prostate of all beyond the age of 50, irrespective of the appearance of symptoms, is the only rational method whereby we may hope to get these cases early.*

EXAMINATION

The routine examination includes rectal palpation of the prostate with a thin-gloved finger, with and without a sound in the urethra. Special attention is paid to perivesical induration, or lateral bands to the pelvic walls. Stricture of the rectum occurs high above the vesicles, as pointed out by Geraghty, and normally can just be reached with the tip of the finger. The superficial lymph-nodes are palpated, as is

also the penis, for carcinoma. Any swelling of the legs is noted.

The amount of residual urine is measured and also the kidney function. Cystoscopy is done. It is not practicable to radiograph the whole body for metastases to the bones. As metastasis most often attacks the lumbar spine and pelvis, one roentgenogram is taken showing both of these. This roentgenogram may also be used to exclude stone of the prostate, the one condition which most simulates carcinoma. I have on one occasion used a long needle inserted through the perineum into the prostate (novocain anesthesia) to make the differential diagnosis between stone and carcinoma. We found that the needle very distinctly grated upon the prostatic stone. Of the 145 cases of prostatic carcinoma seen at the Memorial Hospital, I have never come across a stone in the prostate. And in all of these the prostatic region had been either roentgenographed or needled.

Pathological Examination. Dr. Goeller of our staff has devised a needle which has proved to be of value in the diagnosis of doubtful cases. This needle has a small cutting screw at the point with which prostatic tissue is obtained. The needle is inserted through the perineum (novocain anesthesia) into the prostate, a finger in the rectum guiding it. We have used this needle 33 times, in 16 of which prostatic tissue was obtained, 9 of these cases proving to be carcinoma. It should be used only in cases in which the diagnosis is in doubt.

TECHNIQUE OF RADIUM APPLICATION

1. *Prostate Needle.* The technique first used at the Memorial Hospital in October, 1915, is still with us the most efficient and least painful method of destroying carcinoma of the prostate. A steel needle 10 to 15 cm. long of No. 18 gauge is used, 50 to 100 mc. of radium are placed in the end (terminal 3 cm.) of the needle. Under novocain anesthesia, with a guiding finger in the rectum, the needle is inserted through the perineum into one of the lobes of the prostate. Then at the end of the treatment for that lobe the needle is withdrawn from the prostate (but not entirely out of the perineum) and inserted into the second lobe. A carcinomatous mass 2 cm. in diameter will stand an initial radium

dose of 300 to 400 mc. hrs. This may be repeated in smaller dose in two to three months. We have in certain cases used smaller doses at shorter intervals (25 to 50 mc. every week). But I have no evidence that this method does any more than the above.

2. *Seminal Vesicles—Needles.* The seminal vesicles are radiated routinely if the size of the prostate does not prevent their being reached. Sometimes they are more easily reached through the rectum than by the perineal route, and in some cases we have so radiated the vesicles. A guiding finger is put into the rectum, and a small cannula is inserted up to the vesicles. The needle is put through the cannula, and so into the vesicle. The lower rectum is previously cleansed with soap and water. We have had no infections of the vesicles following this rectal method.

3. *Bare Tubes in Prostate and Seminal Vesicles.* Bare tubes of radium (small doses of radium unscreened except for glass container, and therefore localized and caustic in action) have been used both in the prostate and in any extension beyond the prostate, but have proved not as efficient as the "needle method," and are more painful.

4. *Urethral.* The use of radium in the prostatic urethra has been limited to cases in which carcinoma has directly invaded the urethra. Tubes of screened radium (rubber, 1 mm.; silver, 0.6 mm.) 2 cm. long are attached to a linen thread and inserted into the bladder through the sheath of an urethroscope. The urethroscope is removed and the tubes pulled out into the prostatic urethra by the attached thread. When the treatment is finished the tubes are pulled out of the urethra. Two hundred mc. hours is a maximum dose. This may be varied by using the silver tube of radium in the end of a urethral catheter.

5. *Rectal.* We have treated but a few cases with screened radium in the rectum. This method does not seem to be as efficient as the "needle method" and produces more pain.

6. *Residual Urine.* In most cases the residual urine can be prevented from increasing and in a few it can be decreased by the "needle method" of radium treatment.

If this has no effect and the presence of residual urine causes alarming or intolerable symptoms, we resort to:

(*a*) Bare tubes of radium in the bladder neck. A bare tube of radium (6 mc.) is placed in the end of a flexible needle. This needle, by means of a McCarthy urethroscope or a Buerger operating cystoscope, may be plunged into the prostate at the lower part of the bladder neck. By a plunger the bare tube is pushed out of the needle into the prostate and left there. Its action is local and caustic.

(*b*) If the residual urine does not reduce after this, we resort to the Young punch operation or suprapubic drainage or suprapubic partial prostatectomy.

7. *Pain.* Pain caused by growth of the carcinoma around the pelvic or spinal nerve has rarely reacted to radium or *x*-ray treatment.

8. *Swelling of Legs.* This symptom, caused by pressure of the carcinoma on the common iliac vein, has been successfully combated by the radium pack. This is placed on the abdomen and centered over the vein compressed; from 10,000 to 15,000 mc. hrs. are given.

9. *Rectal Stricture.* I have had 1 case in which I inserted bare tubes (2 of 5 mc. each) into one segment of the stricture. They are inserted through the rectum. This procedure relieved the constipation and made unnecessary a colostomy operation.

RESULTS OF RADIUM TREATMENT

Report of 5 cases of 145 which have gone three to five years after first radium treatment, and have shown regression of the carcinoma.

Case 1. Male, aged fifty-nine. First seen October 15, 1915. Complained of loss of strength and flesh (some 25 lbs.) and night frequency (from 3 to 4 times) for four months. Has had pain in right thigh for five years. Prostatic examination (with Dr. Keyes) revealed a large, hard, fixed, irregular prostate, each lobe as large as an English walnut. The left lobe was more prominent than the right, and there was but little extension toward the seminal vesicles as far as could be felt. No residual urine. A radium needle of 50 mc. was placed in each lobe of his prostate for six hours, on October 20, 1915.

January 14, 1916. The patient has gained about 10 lbs. Examination of the prostate reveals marked shrinking of the carcinoma. Sixty mc. of radium (by needle) was placed for four hours in each lobe of the prostate.

February 18. Did not get up at night to urinate, and had gained 8 lbs. Slight induration at the base of the prostate. Right lateral lobe treated for eight and a half hours with a needle of 30 mc. of radium.

February 27, 1919. Up twice at night, working a full day. Weight the same; 64 mc. of radium in left lobe for six hours.

November, 1919. Up at night, none. Weighs 127 to 130 lbs. Prostate and vesicles feel entirely normal (examination with Dr. Keyes).

January, 1921. Five years and three months after first radium and two years and three months after last radium, prostate and vesicles normal. Patient in excellent condition.

CASE II. Male, aged sixty-six. First seen October 10, 1916. He had night frequency of urination for two years. He now dribbles by night, and urinates every two hours by day. Prostate very large and somewhat irregular, but not suggestive of carcinoma. Residual urine, 1000 c.c. Cystoscopic examination shows a horse-collar prostate. Dr. Keyes did a prostatectomy and Dr. Ewing reported that the specimen showed carcinoma.

November, 1916. Patient had 50 mc. of radium for eight hours in what remained of the prostate.

January, 1917. Increased frequency for the past three or four days. At night urinates every half hour. Prostate feels slightly lumpy in lateral lobe. He had another treatment of radium at this time.

February, 3. Patient had retention of urine, and had to be catheterized three times a day. Radium treatment.

February 27. Patient had complete retention of urine, and a permanent suprapubic tube was put into his bladder.

June 20. Patient has had severe pain in his prostate in the last two months, requiring morphin. The examination shows a prostate irregular, scarred and carcinomatous. The vesicles are indurated, especially the left.

October 15. Patient is in excellent shape physically. He has a collection of calculi around his suprapubic tube. The prostate is flat, the left seminal vesicle has some lumps in it, and is slightly indurated.

January, 1918. Radium in left seminal vesicle and prostate.

April, 1918. Patient is in such good shape that I sewed up his suprapubic opening and he left the hospital emptying his bladder.

June, 1919. In the best of shape (examination with Dr. Keyes). There is the same ridge in the left vesicle, the patient empties his bladder, and his prostate feels normal. He is not treated with radium because it is a question if he has any carcinoma left.

January, 1921. Four years and three months after first radium and three years after last radium, examination the same as in June, 1919. Patient in excellent condition.

CASE III. Male, aged sixty-four. In January, 1916, a prostatectomy was done by Dr. Downes at St. Luke's Hospital. The prstate was found on pathological examination to be carcinomatous. His urethra did not stay open after the prostatectomy, the patient beginning to have increasing retention of urine, and his bladder neck was fulgurated in the attempt to keep the prostatic urethra open. He was first seen by me on April 2, 1917. At that time he had a certain amount of residual urine, but I was unable to get a Phillips' whip into his bladder. Prostate was large and soft. Could not feel above it. There was obstruction in the prostatic urethra. The suprapubic wound drains irregularly. He was treated with 50 mc. of radium in the right lobe for six hours, and was similarly treated in the left lobe.

May 4. Urinates twice at night, and can go five hours without urinating. Before the radium he urinated every one to two hours.

June 5. Sixty mc. of radium in the right and left lobes of the prostate, each six hours.

October 27. Up once at night, and more radium to the right and left lobes of the prostate.

March 1, 1918. Three weeks ago, 50 mc. of radium for seven hours and 15 mc. of bare tubes imbedded in the right side of the prostate. This burned him considerably, and was probably too large a dose.

August 16, 1919. Has a residual of 3 oz. I get a No. 22 French into his posterior urethra. Suprapubic wound still open at times. Urine is very foul.

December 5, 1919. Goes five hours without urinating at night. Very small hard lump in left apex of the prostate. Is it carcinoma? He has had no radium for one year and nine months; the rest of the prostate and vesicles show nothing. He is the picture of health (examination with Dr. Keyes and Dr. Mohan).

April, 1921. Four years after first radium and three years and two months after last radium condition continues excellent. His suprapubic wound leaks at irregular intervals. Residual ½ to 2 oz.

Case IV. Male, aged fifty-five. First seen July, 1917. Urinary frequency has been present for three weeks; by day every hour, by night 6 to 7 times. There is some pain in left groin and testicle and at end of urination. He has lost 10 lbs. in weight. Rectal examination shows a not very large prostate, but very hard and irregular carcinoma running into left vesicle (confirmed by Dr. Keyes). Cystoscopy shows an irregular bladder base and irregular bulging of prostate into bladder. Residual none. A steel needle holding 95 mc. of radium was placed in left prostate for four hours. Lost track of until May 7, 1920. (He had during this interval been operated upon for osteomyelitis of skull.) Prostate feels absolutely normal. Both vesicles sclerosed (confirmed by Dr. Keyes). Urinates once at night and 5 times by day. In excellent health.

May, 1920. Bare tubes of radium were placed in the vesicles.

January, 1921. Three years and five months after first radium and one year after last radium, condition remains excellent and same.

Case V (borderline). Male, aged seventy. First seen in February, 1916. He gave a history of urinary frequency, chiefly at night (3 or 4 times) for the past six months, then acute retention. Patient has lost about 8 lbs. Rectal examination showed a flat irregular prostate with prominent nodules at prostatovesicular junction extending into the vesicles. He was treated several times with radium needles through the perineum. He had no more attacks of retention, his general health improved, and his prostate remained soft and irregular but showed nothing to justify treatment.

December, 1919, the left vesicle seemed slightly enlarged, and radium was recommended as it was feared the growth might be carcinoma. The prostate was flat and soft.

August, 1920, patient had an attack of severe pain in the back and left side and was confined to bed. I saw him then when he looked near death, and was confined to bed with what was thought to be involvement of his spinal cord by the carcinoma. His prostate felt as normal as in December, 1919.

January, 1922, reported up and well.

In these 5 inoperable cases the prostates and vesicles are somewhat irregular, scarred, but otherwise normal. They are the only cases which have gone a sufficient length of time since their first and last treatments to report. They all show marked regression of the disease.

Results in 2 Cases in Which the Carcinoma Was Confined to the Prostate Out of 145 Cases Seen

Case I. Male, aged sixty-one. First seen in August, 1919, with a history of dysuria for fifteen months, a small urinary stream, and frequency of urination, and then finally complete retention. He came to the Memorial Hospital from Bellevue Hospital with a retention catheter in his bladder. His prostate was hard, regular, the size of an English walnut. No induration around the seminal vesicles.

September 5. By means of the cystoscope, a bare tube of radium of 6 mc. was placed in the median lobe of his prostate.

September 23. The residual had fallen to 1 oz., and he got up 2 to 4 times at night to urinate, and at times during the day goes four hours without having to urinate. Because of some lumps in his prostate, more radium in the form of bare tubes was applied on September 30. Following this treatment he began urinating every half-hour by day and night notwithstanding the fact that his residual urine was only half an ounce. He became steadily worse and finally died uremic. He had chills and fever for a couple of weeks before his death. Death was probably due to infection from his prostate and to uremia.

Case II (borderline). Male, aged seventy-one. First seen December, 1919, with a history of hematuria nine months previous. Following this he had frequency of urination and urgency. When seen his night urination was 6 to 7 times. Urine has been steadily bloody, for the past forty days. Residual urine, 2 oz. His prostate was as large as a hen's egg, a hard single lump. No enlargement around the seminal vesicles. He has had 2 treatments of radium needles in prostate. The growth has very markedly gone down. Patient is still under treatment.

SUMMARY

One patient died uremic, and the second is still under treatment.

Result in Very Extensive Carcinoma of the Prostate with Complete Regression of the Carcinoma (Post-mortem Report)

Male, aged fifty. First seen at the Memorial Hospital, August 23, 1919. Three weeks previous, partial resection of the bladder for carcinoma was done at another hospital. The carcinoma of the bladder was presumably secondary to a carcinoma of the prostate. When the patient was first seen the prostate was

very hard, the size of a tangerine, with a number of very hard nodules in it. The vesicles and the base of the bladder were involved by growth. He came to the hospital with a suprapubic drain. Cystoscopy showed a recurrence at the site of the bladder resection. He was treated with radium and lost track of up to January, 1920.

January, 1920. Had a recurrence in the abdominal incision—3 large lumps, each the size of an English walnut, which were treated with bare tubes of radium. He was almost exsanguinated because of hematuria, and his bladder was again treated with radium.

February, 1920. Had a carcinomatous mass from the symphysis to the anterior superior spine on the right side. On the left side was a mass in the inguinal region 8 cm. wide from the symphysis midway to Poupart's ligament, an enormous carcinoma of the lower abdomen. This was treated with radium.

May, 1920. All the abdominal masses had entirely gone and his prostate was markedly shrunken.

November. He went on an auto trip, became chilled, and could not void. An outside doctor tried to pass catheter; ten days later the patient died.

Post-mortem examination showed the following (Dr. Ewing):

"A section from various portions of the bladder, prostate, pelvis and lumbar lymph-nodes failed to show any trace of carcinoma. The walls of the main bladder cavities were everywhere lined with a slough which was very extensive, a diffuse phlegmonous inflammation. The lungs showed purulent bronchitis and pneumonia; the kidney, acute nephritis; prostate, necrosis."

Results in Suprapubic Prostatotomy to Relieve Retention

This operation has been done in the following way:

Through a suprapubic opening the lower part of the bladder neck has been bitten out with a long rongeur forceps. The operation, aside from using the forceps to bite out the carcinoma, is done precisely in the same way that a suprapubic prostatectomy for adenoma is performed. I have done it only in cases of urinary retention (generally complete) which could not be managed by catheter or which could not be overcome by any of the other described methods. In all cases in which it was done the carcinoma was very advanced. Eight cases in all have been operated upon. Seven cases left the hospital after operation, 1 died in the hospital two months after operation from the growth of the carcinoma around the ureters and failing kidneys. Three were lost track of after they left the hospital. Two patients went two years and three months emptying their bladders, and then died. One of these had partial daily incontinence of urine. Wherever practicable the prostate had been thoroughly radiated for a number of months previous to the operation.

Results in Cases Treated by Radium Needle in Prostate in which Residual Urine Has Not Varied over a Number of Years

Case I. No residual, October, 1915. Treated by needle in prostate, never any residual to January, 1921.

Case II. No residual, but one attack of acute retention, February, 1916. Radium needles in prostate, never any residual and no attacks of retention up to August, 1920.

Case III. Operation removed carcinoma from bladder neck secondary to prostatic carcinoma, May, 1916. Radium needles in prostate. Up to April, 1919, no residual urine.

Case IV. Operative removal of carcinoma of prostate, October, 1916. Several acute retentions followed this. Then retention catheter. Radium needles in prostate. From April, 1918, to January, 1921, no residual urine.

Case V. Residual 6 to 8 oz., October, 1917. Radium needles in prostate. April, 1918, residual 1½ oz. January, 1921, residual again 8 to 10 oz.

Case VI. Residual, April, 1917, could not be determined as no instrument could be introduced into bladder. Radium needles in prostate. August, 1918, to January, 1921, residual 1 to 3 oz. A No. 22 French catheter may be introduced into bladder.

Case VII. No residual, July, 1917. Radium needle in prostate. No residual, January, 1921.

These are 7 out of the first 43 cases (in 1916 and 1917) which are still living, and which have been observed long enough to give an accurate idea as to the effect of radium on maintaining the capacity of the bladder to empty itself. In none of them has the residual urine increased and in 1 (Case VI) it probably has decreased.

Results of Radium (Bare Tubes) in Bladder Neck to Reduce Residual Urine

Case 1. April, 1918, residual urine 260 cc. He had 7 mc. (bare tubes) of radium applied in the lower part of bladder neck. In July, 1918, he had no residual urine.

Case II. September 1, complete retention for a number of weeks. Retention catheter September 5. A bare tube of radium 5 mc. in bladder neck. September 23, residual urine 1 oz. October 21, residual urine ½ oz.

Case III. Complete retention for two weeks. Retention catheter. Bare tubes of radium 6½ mc. in bladder neck. Five days later he emptied his bladder and continued to do so for six months.

We have tried this method in 4 other cases with no effect on the residual urine. It is a procedure not without danger,

as one patient who had an extensive carcinoma of the prostate with foul urine and complete retention died two weeks after bare tubes were placed in the bladder neck. He died outside the hospital.

Before the tubes are applied the patient's bladder should be made as clean as possible, and the kidney function determined. He should be in the hospital.

Young Punch Operation. This has been performed in 4 cases; in 2 without success; one patient went from a complete retention of urine to 1 to 2 oz. of residual urine, but died two weeks after the operation from infection of his kidney. The fourth patient left the hospital emptying his bladder within 1 oz. One year later he was heard from, and at that time the suprapubic fistula had reopened, so the success of the operation could not be determined.

Summary of Methods to Reduce Residual Urine in Carcinoma of the Bladder. Sometimes the needle method in the prostate reduces the residual urine; sometimes the bare tube in the bladder neck does this, but this method is accompanied by considerable pain and some danger. Occasionally the Young punch operation works, as does nearly always the major operation—the suprapubic cutting out of the lower part of the bladder neck. The problem is the most difficult one we have to deal with, and the ideal procedure in intractable cases has not yet been found.

Results in Reduction of Swelling of the Legs Caused by Metastatic Carcinoma

We have had 2 cases in which, by means of a radium pack, the swelling of one or both legs has been reduced. In one of these patients who had swelling in one leg and considerable disability, the swelling reduced one month after the radium pack, and the patient lived in comparative comfort until he died of a cerebral thrombosis. In another patient who had swelling of both legs and edema as far as the umbilicus, the application of one radium pack over the right lower abdomen succeeded in reducing the edema within one week after its application. Both of these cases had very extensive carcinoma of the prostate and no attempt was made to treat the carcinoma itself.

CONCLUSIONS

1. In but 2 per cent of cases of carcinoma of the prostate seen at the Memorial Hospital is the carcinoma apparently confined to the prostate.

2. Routine prostatic examination of all patients beyond the age of fifty, irrespective of symptoms, is the only rational method whereby we may hope to make a diagnosis of prostatic carcinoma early in the disease.

In all doubtful cases a specimen of the prostate for pathological examination should be obtained with the specimen needle.

3. The results of radium treatment of carcinoma of the prostate are superior to operative removal both in causing regression of the disease and in coping with urinary retention.

XV

RADIUM TREATMENT OF CARCINOMA OF THE BLADDER[1]

BENJAMIN S. BARRINGER, M.D.

The treatment of carcinoma of the bladder at the Memorial Hospital has been divided into two periods, viz., that prior to June, 1919, when we were testing what could be done with radium applied through the urethra and without opening up the bladder; and that period since June, 1919, during which we have added to the intraurethral treatment the application of radium through the bladder opened suprapubically. The object of this latter phase was to destroy extensive bladder carcinomas which we had not been able to cope with through the urethra. The results of both these forms of treatment are herein reported and this paper is based upon all cases seen at the Memorial Hospital up to January, 1921, a period of nearly five and a half years: 142 cases of advanced carcinoma; 4 cases of small carcinoma; 9 cases of extensive papilloma; 2 borderline cases.

PATHOLOGY—CLASSIFICATION

In 53 cases of tumor of the bladder the pathological examination (Ewing) was as follows: Papilloma, 7 cases; papillary carcinoma, 18 cases; infiltrating carcinoma (variously called epidermoid carcinoma, malignant epithelioma, papillary infiltrating carcinoma), 22 cases; adenocarcinoma of prostatic type (alveolar carcinoma), 4 cases; papillary adenocarcinoma, 1 case.

I can see no reason for making another class, "malignant papilloma," which means that a tumor purely papillomatous in histological structure, either by its rapid growth or rapid recurrence after removal, shows more malignant tendencies

[1] Reprinted from *Ann. Surg.*, Dec., 1921, lxxiv, No. 6, pp. 751–767.

than the usual papilloma. The term "malignant papilloma" refers to a clinical rather than a histological difference. In these 52 cases there was but one which could not be classified under the above heading, that of papillary adenocarcinoma. The 4 cases of alveolar carcinoma were probably secondary to a prostatic carcinoma.

Papillary Degeneration into Carcinoma

There has been much written on the fact that papilloma may remain such for a long period and then take on a carcinomatous degeneration. (Mandlebaum. The pathology of new growths of the bladder. *Surg., Gynec. & Obst.*, September, 1907: Buerger. *Trans. of A. U. A.*, 1915.) The basis for this rests upon two findings:

1. Clinical; a pure bladder papilloma may be observed at one time (cystoscopically and by pathological specimen) and a number of years later a well-developed carcinoma be identified.

2. Pathological; the fact that a tumor shows in one part pure papilloma and in another part carcinoma may indicate that a benign papilloma has become carcinomatous.

We have seen patients with extensive papillomata of the bladder with histories dating back four, five, six years and more which showed at the time of examination no malignant changes (pathological examination, Ewing) and which had no induration at the base of any of the multiple tumors. We have also seen patients with carcinoma of the bladder (identified pathologically and cystoscopically) live for a number of years with their carcinomas. Our observations lead us to believe that many bladder tumors run true to their original histological structure. Many papillomata begin and end papillomata, and many carcinomas begin and end as such. We must, however, not forget that malignant degeneration may take place in a papilloma and therefore papillomata are potentially malignant.

History. Age first seen—125 cases (121 extensive carcinomas, 4 small carcinomas). Twenty to thirty years, 3 cases; thirty to forty years, 16 cases; forty to fifty years, 20 cases; fifty to sixty years, 37 cases; sixty to seventy years, 35 cases; seventy to eighty years, 14 cases.

The fifth and sixth decades showed the greatest incidence of carcinoma. Nine extensive papillomas of the bladder gave 4 cases between fifty and sixty; 2 cases between sixty and seventy; 1 case between seventy and eighty; so giving about the same age incidence as carcinoma.

Duration of Symptoms. One hundred and twenty-one cases (116 advanced, 5 early carcinomas). One to three months, 15 cases; three to six months, 14 cases; six to twelve months, 35 cases; twelve to eighteen months, 9 cases; eighteen to twenty-four months, 16 cases; twenty-four months, 32 cases.

These tables emphasize that most patients with carcinoma of the bladder have symptoms for a year or more before their condition is seriously considered. If they could be seen earlier very many more could be cured.

Among the cases of extensive papilloma was one with symptoms dating back six years; he had extensive solid papillomas almost filling the bladder. There was no induration of the base of any of these; pathological examination (Ewing) showed papilloma. One extensive carcinoma of the bladder had bladder symptoms dating back fourteen years.

Sex. One hundred and fifty-three cases (male, 119; female, 34). This preponderance of males may signify that inflammation may be a causative factor in carcinoma of the bladder. Prostatitis and trigonitis (gonorrheal) have no analogue in the female.

Loss of Weight and Strength. Of 126 cases (124 advanced carcinoma) 39 cases showed a decided loss of weight. Loss of both weight and strength is commonly supposed to be an accompaniment of malignant disease. These two as a symptom of bladder carcinoma generally appear late. In our records there are a good many cases of bladder carcinoma, too advanced for any therapy, which have kept both their weight and strength up to the time when seen. If the loss of weight be due directly to the carcinoma and not secondary as e.g., serious infection of the kidneys, then one may suspect that the carcinoma has grown beyond the bladder.

First and Second Symptoms. One hundred and thirty-eight cases (135 advanced carcinoma, 3 small carcinoma).

Hematuria. First symptom, 70 cases; second symptom, 60 cases; no hematuria, 8 cases. This symptom of tumor of the bladder therefore appeared in 130 out of 138 cases. In recognizing this as a cardinal symptom in early cystoscopy and appropriate treatment thereafter lies the solving of the question of carcinoma of the bladder.

In 8 extensive papillomas of the bladder, but 1 gave no history of hematuria.

Disturbance of Urination. One hundred and eighteen cases (116 advanced carcinoma, 2 small carcinoma); first symptom, 58 cases; second symptom, 52 cases.

The carcinoma in the majority of cases causes some urinary disturbance: Frequent urination, dysuria, polyuria, retention, incontinence.

Loss of Weight (116 cases). First symptom, no cases; second symptom; 5 cases. Loss of weight comes on late in the disease.

Pain Down Leg (116 cases). First symptom, no cases; second symptom, 3 cases.

This symptom so often seen in prostatic carcinoma is comparatively rare in bladder carcinoma and is almost always an index of nerve involvement by the carcinoma beyond the bladder.

EXAMINATION

Cystoscopy: (1) Presence of tumor. (2) Carcinoma or papilloma. Usually the cystoscopic diagnosis is not difficult. If there is fresh bleeding, the best view of the bladder and tumor is made during irrigation. The red, fluffy papilloma may be confused with blood clots, and the gray, sloughy carcinoma with calcareous incrustation of the bladder. The examination of pieces of tumor obtained with the rongeur forceps (cystoscopic) or sticking to the cystoscope may confirm the diagnosis. Pieces of the white, sloughy portions of a tumor usually show nothing diagnostic microscopically.

Carcinoma or Papilloma. It probably falls to our lot at the Memorial Hospital to see more carcinoma than papilloma. In five years we have seen very few, not more than five or six, papillomas which have been suitable for destruction by fulguration.[1] We have also seen many patients whose

[1] These are not included in the present report.

tumor has been fulgurated at length and often before they came to us with full-blown carcinoma. Extensive tumors of the red papillary type should be suspected of being carcinomatous, notwithstanding the oft-returning pathological report "papilloma." The more a tumor tends toward the flat type, the more malignant is it.

A raised thickened base means carcinoma. All sloughy tumors are carcinomatous.

Rectal Examination. If there is extensive induration of the bladder base, that is an indication that the tumor has grown through the bladder. If the tumor or its base is felt, but between the tumor and the examining finger is interposed somewhat soft bladder wall, the case is still suitable for exploration. In a number of such cases we have removed the tumor from the bladder for various periods of time. The examination should be made with a thin-gloved finger, and the bladder must be empty of fluid.

Residual Urine. This is rarely present if the prostate is not primarily involved and should always suggest the possibility of prostatic involvement.

Kidney Function. In 10 out of 15 cases (operated upon) the kidney function was reduced. In a few instances this reduction was marked, the lowest phenolsulphonephthalein output being 5 per cent in the first hour and 7 in the second. This reduction in kidney function, which occurs in perhaps 2 out of 3 cases of carcinoma of the bladder, is of importance in determining the length of the operation, the kind of operation and the prognosis. We have had three interesting kidney conditions following the use of radium.

Case I. Male, who had an infiltrative carcinoma of the right side of the bladder near the right ureter orifice. This was small and operable. It has been destroyed by radium now for four years. He also had retention of urine and a hypertrophied prostate. In the midst of his radium treatment he had a stormy time with retention of urine and pyuria. About a year ago it was determined that his kidney corresponding to the side occupied formerly by the carcinoma was a pyonephrotic sac. Either the carcinoma encroaching upon the ureter or cicatrization by the radium caused this kidney's destruction.

Case II. Female, who had an extensive carcinoma of her bladder around the right ureter. Previous to radium treatment she had several very severe attacks of renal colic on the side corresponding to the tumor. For ten months subsequent to radium treatment she had no more attacks of renal colic. The tumor

was by no means entirely gone, but apparently that portion around the ureter orifice was destroyed, relieving her of the attacks of colic.

Case III. Male, who had an extensive papilloma of the right side of his bladder. He had previous to operation a phenolsulphonephthalein output of 5 per cent the first hour, and 7 the second hour. His bladder was opened suprapubically, the tumor snared off and radium imbedded in the base. For a number of weeks he ran a slight temperature, then considerable temperature, and was found to have a large right kidney. His condition became progressively worse. I opened his kidney under novocain and found it to be hydronephrotic with the urine under tension and with pus in the kidney pelvis. This was drained and the patient became better for a number of weeks, then died septic.

Cystogram. We have used the following technique at the Memorial Hospital to show graphically the tumor and the infiltration of the bladder wall. The patient is placed flat on his back, a catheter is introduced into his bladder, and the contents emptied. With a large syringe the bladder is blown up with air until the patient feels discomfort. The roentgenogram is immediately taken without withdrawing the catheter from the bladder. We have in many cases compared the findings on opening the bladder with the results shown by cystogram, and find that in most cases they quite accurately correspond. If a tumor is pedunculated its pedicle is not shown by cystogram.

Secondary Urethral Tumors. We have seen a good many cases of urethral tumors either accompanying or following bladder tumors. I think we often overlook these small urethral tumors, having our eye on the major condition. Whether they are real implantations from the bladder or a retrograde lymphatic invasion, I hesitate to say. Most of these urethral implants are of the same structure as the bladder tumor, although I have lately seen a small soft urethral tumor in a patient in whom I had removed an indurated carcinoma from his bladder. I think it safe to consider them as malignant as the bladder tumor.

INDICATIONS FOR RADIUM

1. *Local Removal from Bladder.* If the tumor is confined to the bladder it may be suitable for removal by radium. We have removed from the bladder (for various periods of time) all kinds of carcinomas, viz., infiltrating, indurated, exten-

sive, highly malignant.[1] This naturally does not mean that we have been uniformly successful; far from it. Different tumors react differently to radium.

2. *Hematuria.* Radium fairly consistently controls hemorrhage, and may be used for this even if the tumor has gone beyond the bladder.

3. *Retarding the Growth of Tumor.* The question is often asked: "Even if there is no hope of cure, will not radium retard the tumor growth so that a patient may live longer and more comfortably?" Undoubtedly this is true now and again. The cases in which radium does this are so few, however, the failures so many, that I believe it unwise to give radium therapy in those cases in which there is no hope of removing the tumor from the bladder.

Reaction of Different Tumors to Radium. Different papillomas showing precisely the same structure microscopically react differently to radium—some are destroyed easily and some resist. The same is true of papillary carcinoma, although as a rule papillary carcinoma seems to be more sensitive to radium than papilloma. Papillary carcinoma can be destroyed by surface radiation (using large doses of screened radium). Indurated carcinomas are best destroyed by implanting throughout the indurated area small bare tubes of radium into the base of a tumor and leaving them there. These bare tubes are very caustic, and very local in their action, extending over an area of about 1 c.c. In using them even with great accuracy it is possible to miss some carcinomatous area. Therefore we use a combination of the bare tubes (in the depth) and the screened radium (in the surface) in every case of indurated carcinoma.

DETERMINATION OF METHOD OF RADIUM TREATMENT

I. *Intravesical.* Growths confined to and around bladder neck. Papillomata. Pedunculated papillary carcinoma if pedicle can be reached. Infiltrating sessile growths of no more than 2 cm. in diameter.

II. *Suprapubic.* Growths other than the above and without metastasis. Extensive infiltration of the bladder wall,

[1] The largest infiltrating tumor removed was as large as a hen's egg; had grown through the bladder wall and was adherent to the symphysis (Case II).

large and multiple tumors are the indication for section, to which all doubtful cases are submitted.

Intravesical Methods. By means of a flexible spring holder used through the sheath of the Brown Buerger operative cystoscope 100 or more mc. of unscreened radium may be held up against the tumor for the period of half an hour while the tumor is being observed through the cystoscope. This may be repeated every two weeks, or less often if the tumor is disappearing satisfactorily. If the tumor looks solid or hard,

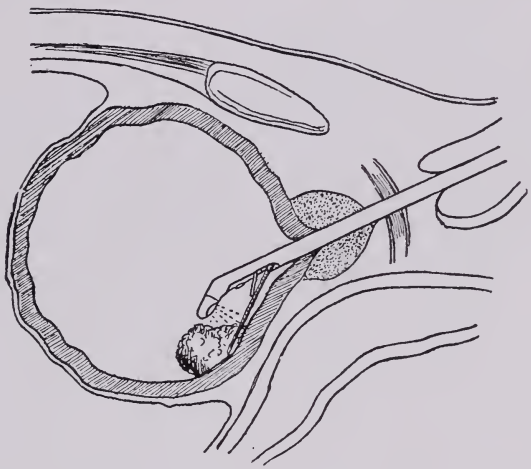


FIG. 35. Method of burying radium emanation tubes in growth by means of special introducer and the cystoscope.

or has a base which looks indurated, then we may treat it by thrusting into its base or the indurated part a radium needle screened simply by the steel of the needle. This needle is also on a flexible spring and is used through the operating cystoscope. Needles from 50 to 200 may be used for a period of time up to forty minutes. We must remember that in this method the action is local and caustic. We have in a similar way implanted small bare tubes of radium into the base of a tumor and left them there. For this, bare tubes of 0.5 mc. to a sq. cm. of tumor are used, and left in place. The action here is still more local and more caustic. We have used all these methods and combinations of them in various tumors

and by all of them have destroyed small or recurrent carcinomas of the bladder. If a tumor is more extensive, if it is papillary in character, if the pathological examination shows pure papilloma, and especially if it be around the bladder neck, we often start the treatment by placing in the bladder two tubes of screened radium (0.6 mm. silver, 2 mm. rubber). These tubes are inserted through the sheath of a straight cystoscope, tied with a string and left in place for varying periods of hours and then pulled out of the urethra by the

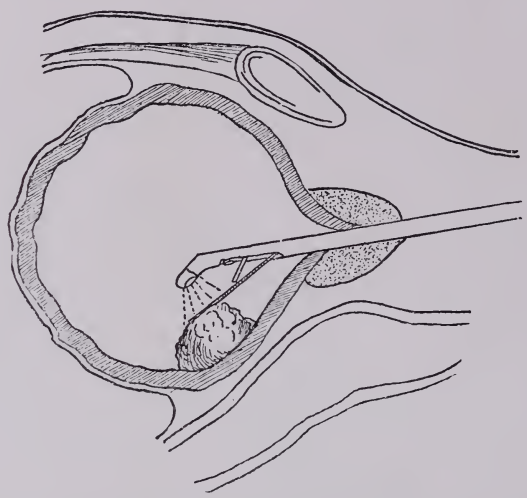


Fig. 36. Surface application of radium emanations to growth under vision by means of special applicator in cystoscope.

attached string. As a rule we use two tubes of 50 mc. for five or six hours. The value of such radiation is: First, to see how the tumor reacts to radium; second, to stop temporarily the bleeding to make cystoscopy possible; and third, to destroy that portion of the tumor around the internal urethral orifice. If the tumor is carcinomatous and large, and we believe from our examination it is confined to the bladder, then we do the open operation described below.

Suprapubic Application of Radium in Extensive Carcinoma. Because we were unable to cope with extensive carcinomas of the bladder by the intraurethral method, we began, in June, 1919, to open up the bladders in selected cases and implant

radium directly into the carcinoma. The technique is as follows:

Gas and oxygen anesthesia is used. The bladder is prepared previous to operation by washing it out with a 1:4000 acriflavine solution, then draining the fluid out of the bladder and blowing the bladder up with air. The patient is placed in Trendelenburg's position. The skin incision is a long one, extending from the symphysis to the umbilicus. The prevesical fascia is cut transversely at the symphysis and dissected

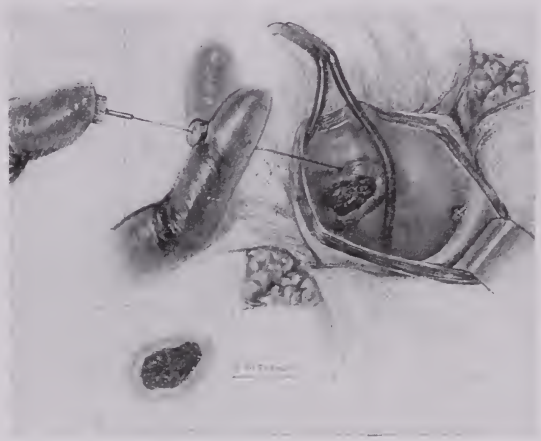


FIG. 37. Burying radium emanation tubes under direct vision after exposure of carcinoma by suprapubic cystotomy.

back, the bladder being exposed well down its posterior wall. The urachus is cut, and the exposure extends beyond this. The sides of the wound are screened with gauze soaked in acriflavine (1 to 4000) solution. The bladder is gently palpated so that the incision may not go through tumor tissue. Between two clamps the bladder is opened and a three- or four-inch incision is made longitudinally. The cut surface of the bladder is grasped by clamps, the clamps being about one inch apart. The reason for this is that the bladder will otherwise collapse and fall down into the pelvis when retractors are put into it, making operation impossible. A light is thrown into the bladder and bladder retractors, three or four in number, are gently placed in the bladder. The retractors which we have used most have been made for us at

the Memorial Hospital. They are made of one-eighth-inch steel wire in the form of an open loop. The advantage of these is that the tumor may be seen through the open portion of the retractor, and treated. The tumor being exposed is sponged as little as possible to prevent bleeding and spreading of tumor cells. Alcohol sponges are used. Any protruding portions of the tumor are snared off, using a simple wire snare.

FIG. 38. Use of special retractor in exposing clearly the carcinoma, especially its base. Snaring off pedunculated growth preparatory to burying radium emanation tubes in its bore.

If the tumor is flat and not papillary in type, none of it is removed. The reason for snaring off the papillary part is better to expose and treat the base. Indurated parts of the tumor are implanted with radium bare tubes (0.5 mc.) by means of a needle, using two of these to the square centimeter. These bare tubes are not put in the normal mucous membrane, but within a quarter of a centimeter of the edge of the tumor. Finally, surface radiation is accomplished by means of tubes of radium screened by 0.6 mm. of

silver and 2 mm. of rubber placed on the surface of the tumor and held in place either by gauze packing or little hooks on the silver tubes. A string is attached to these tubes, and they are pulled out after an appropriate time. A space 2½ c.c. in diameter is radiated by two of these tubes placed longitudinally side by side, 1 cm. apart. To such an area, 500 or 600 mc. hrs. is given. Before placing these tubes, a can of ether is emptied into the bladder to kill any stray tumor cells. The bladder is closed up with plain catgut, the strings of the radium tubes and the packing passing through the small opening left in the bladder. The gauze screening in the wound is now removed, and ether poured all over the wound. The wound is closed as usual. Two cases operated upon in this manner are here reported to show what can be done in inoperable (aside from total cystectomy) cases.

Case I. Male, aged thirty-seven. In 1917, nocturnal frequency of urination progressively increasing until he urinated every fifteen minutes. Never hematuria.

In November, 1917, a small carcinoma of the bladder was excised. It recurred very rapidly. Shortly after leaving the hospital his frequency was as great as before.

In June, 1919, he came to the Memorial Hospital with complete retention of urine and had to be catheterized. I opened his bladder and found it full of clots and a red papillary carcinoma the size of a small orange attached to the left bladder base and lateral wall. The papillary portion of this was cut off with a cautery, and fifteen bare tubes of radium (3 mc. each) were planted in the base of the tumor, which was of the size of a silver dollar and which included the opening of the left ureter. A suprapubic tube was left in for a number of days, then removed, the wound healing without trouble. He had burning and frequency for a number of months after operation caused by the radium. Cystoscopy, February 25, 1920, showed a bladder clean of tumor. There was no induration of its bladder base by rectal examination. He had gained 39 lbs. in weight and was working all the time.

In January, 1921, cystoscopy showed a clean bladder with one or two very small papillomas of his posturethra. These were treated by radium.

Case II. Male, aged sixty-two. A single hematuria in January, 1920, then clear urine and again, February, hematuria. At this time he was cystoscoped and the diagnosis of "tumor of the bladder" made.

I first saw him in March, 1920. Then he was a well-nourished man, had lost no weight, had a nocturnal urinary frequency of two. He passed urine colored with blood. The rectal examination showed slight induration of the middle of the bladder base with a normal prostate. The cystoscopic examination showed a tumor on the right side of his bladder, sloughy on the surface. It was impossible to tell its extent because of the hematuria. He gave a history of having had sugar in his urine but his blood sugar was not increased. He was but a fair

EXTENSIVE CARCINOMA OF BLADDER—RADIUM IMPLANTED THROUGH BLADDER OPENED SUPRAPUBICALLY

No.	Name	Age	Date oper.	Description of tumor	Pathology	Previous oper.	Result
1	V.	36	June 1919	Papillary tumor, large as orange, base 5 × 5 cm., of left bladder base	Papillary infiltrating carcinoma (Ewing)	One	Bladder clean (cystoscopy) 20 mos. post-op. (sl. papilloma of urethra)
2	K.	54	Jan. 1920	Papillary tumors, indurated base (largest 3 × 3 cm.) all around bladder neck	0	0	Bladder clean (cystoscopy 9 mos. post-op.
3	W.	61	Mar. 1920	Solid tumor, ulcerated surface (6 × 6 × 6 cm.) on anterior wall of bladder, growing through bladder and adherent to pelvis	0	0	Bladder clean (cystoscopy) 12 mos. post-op.
4	W.	60	Apr. 1920	Pedunculated tumor (small tangerine) covered with incrustations, left bladder wall, indurated base	Papillary carcinoma (Ewing)	0	Bladder clean (cystoscopy) 9 mos. post-op.
5	G.	50	Apr. 1920	Solid, flat tumor 3 × 4 cm., within 1 cm. of left ureter	Infiltrating carcinoma (Ewing)	0	Recurrence after operation treated intravesically Bladder clean (cystoscopy) Feb., 1921
6	D.	33	May 1920	Solid tumor, left wall, 2 × 4 cm. Papillary tumors around bladder neck	Infiltrating carcinoma (Ewing)	0	Recurrence after operation. Treated intravesically (3 times). Mar., 1920, no tumor. Radium slough

7	T.	59	June 1920	Flat, irregular tumor around urethra (treated by radium before oper.). Small tumor seen at oper.	Infiltrating carcinoma	0	No tumor 6 mos. post-op. Radium slough (cystoscopy)
8	S.	55	July 1920	Papillary tumor, 4 × 5 cm., of left bladder base. Base indurated	Papillary carcinoma (Ewing)	0	Bladder clean (cystoscopy) 9 mos. post-op.
9	W.	50	Aug. 1920	Indurated, ulcerated tumor, 3 × 3 cm., around sphincter of bladder	Epidermoid carcinoma (Ewing)	0	Bladder clean (cystoscopy) 6 mos. post-op.
10	R.	70	Dec. 1920	Indurated, flat, irregular tumor, 3 × 3 cm., centering in l. trigone & touching bladder neck	Papilloma (Ewing)	0	Bladder clean (suprapubic observation) 2 mos. post-op.
1	H.	48	Sept. 1919	Number of hard nodules around bladder base. (Scar of radium in bladder neck from pre-op. treatment)	Papillary carcinoma (Brooklyn Hospital)	One	Eighteen mos. post-op. has sl. urinary frequency (once at night). No pain. Looks and feels entirely well. Refuses cystoscopy
2	H.	56	Sept. 1920	Papillary tumor 6 × 4 cm. posterior to l. ureter. Pedicle infiltrated. Base 3 × 3 cm.	Papilloma (Ewing)	0	Recurrence post-op. Still treated (Mar., 1920)
3	B.	49	Oct. 1920	Multiple hard tumors, bladder base & anterior wall; one 2 × 3 × 2½ cm.; one 3 × 1 × 1 cm.	Carcinoma (Brooklyn Hospital)	One	Not cystoscoped post-op.
4	M.	50	Dec. 1920	Indurated ulcerating tumor touching internal urethra 4 × 3 cm.	Squamous infiltrating carcinoma (Ewing)	0	Note cystoscoped post-op.

EXTENSIVE CARCINOMA OF BLADDER—RADIUM IMPLANTED THROUGH BLADDER OPENED SUPRAPUBICALLY (*Continued*)

No.	Name	Age	Date oper.	Description of tumor	Pathology	Previous oper.	Result
5	R.	..	.....	Solid, rounded, nonpedunculated tumor, indurated base, touching left side trigone, 7 × 10 cm.	Papillary carcinoma (Ewing)	0	Not cystoscoped post-op.
1	R.	59	July 1919	Whole bladder wall carcinomatous, not treated	0	0	Died 5 mos. later
2	H.	42	July 1919	Extensive indurated carcinoma 10 × 5 × 2 cm., probably originating in prostate	Epidermoid carcinoma (Ewing)	0	Died 6 mos. later
3	R.	47	July 1919	Indurated carcinoma around bladder neck, probably primary in prostate	Papilloma (Ewing)	0	Died 14 mo. later of anuria after pyelotomy to relieve obstruction of lower ureter caused by carcinoma
4	W.	41	Aug. 1919	Extensive growth of bladder wall, coming from outside bladder (?)	0	0	Died 1 yr. later
5	C.	60	Dec. 1919	Entire vault and sides of bladder infiltrated. Trigone clear	Infiltrating epidermoid carcinoma (Ewing)	0	Died 3 mos. later
6	L.	38	Dec. 1919	Extensive, diffuse papillary tumor of anterior wall	Papillary carcinoma (Ewing)	0	Died at another hospital (3 mos. post-op.) from infarction of prevesical space due to sloughing of bladder wall by radium
7	S.	52	Feb. 1920	Indurated carcinoma (3 × 3 cm.) around internal urethra	0	0	Died 7 mos. later

8	L.	60	Apr. 1920	Mass size of golf ball, touching internal urethra base, 2 × 10 cm.	Carcinoma (Ewing)	0	Died 2 mos. later
9	D.	69	Apr. 1920	Pedunculated tumor 8 × 4 cm. (base 3 × 3 cm.) attached to trigone	Papillary carcinoma (Ewing)	0	Died of uremia 7 wks. post-op. Bilateral pyonephrosis
10	B.	43	Apr. 1920	Papillary carcinoma with indurated base (7½ × 4 cm.) touching right ureter	Papillary carcinoma (Ewing)	0	Operated upon twice. Now 6 mos. after 2d operation has urinary frequency, but is in fair general condition
11	R.	49	Apr. 1920	One carcinoma, lateral wall, 5 × 5 cm. × 1 cm. (thick); 1 carcinoma left trigone & urethra, 7 × 1 cm.	Infiltrating squamous carcinoma (Ewing)	0	Left hospital in good shape. Cannot be traced since
12	O.	50	Apr. 1920	Two sloughy tumors, 2½ × 1 cm. and ¾ × ½ cm.	Alveolar carcinoma (Ewing)	Once	Doing badly. Implantation in abdominal wound (Mar., 1921)
13	B.	60	May 1920	Flat, indurated carcinoma, 10 × 7 cm.; implant 1 × 1 cm.	Solid carcinoma (Ewing)	0	Died 3 mos. post-op.
14	E.	56	Aug. 1920	Sloughy, flat carcinoma, right bladder wall, 3 × 3 cm.	Carcinoma (Ewing)	0	5 % sugar in urine at time of operation. Died 3 mos. post-op. of perirectal abscess

No.	Name	Age	Date oper.	Description of tumor	Pathology	Previous oper.	Result
1	W.	55	May 1920	Firm, red, papillary tumor, large as small orange, base 3 × 3 cm., external to left ureter. A second small tumor.	Papilloma (Ewing)	0	Bladder clean (cystoscopy) 10 mos. post-op.
2	Mc.	61	Oct. 1920	Tumor large as tangerine (calcareous incrustations), right lateral wall, base 2 × 2 cm. No induration base	Papilloma (Ewing)	0	Five mos. post-op. no tumor (cystoscopy). Radium slough
1	W.	55	Apr. 1920	Bladder filled with papillomata; no induration of bases	Papilloma (Ewing)	One	Seven mos. after 1st operation was operated upon 2d time for suprapubic sinus & more papillomata. Still treated (Mar., 1921)
2	C.	56	May 1920	Very large papillary tumor 7 × 7 × 7 cm., attached to bladder base, posterior to left ureter, base 4 × 4 cm.	Papilloma (Ewing)	0	Reports well 9 mos. post-op. Not cystoscoped post-op.
3	P.	63	June 1920	Entire bladder base & lateral walls covered with papillomata; no induration	Papilloma (Ewing)	0	Six mos. post-op. still papillomata. Being treated

4	K.	56	Oct. 1920	Pedunculated tumor, 5 × 4 × 3 cm. anterior to r. ureter; no induration	Papilloma (Ewing)		Not cystoscoped post-op.
5	S.	48	Dec. 1920	Entire lower half bladder filled with papillomata; no induration	Papilloma (Ewing)	0	Not cystoscoped post-op.
1	B.	56	Sept. 1920	Three papillomata, bladder base, largest 4 × 4 cm.; no induration	Papilloma (Ewing)	0	Died 3 mos. post-op. Pyemia (after pyelotomy for pyonephrosis)

CARCINOMA OF BLADDER TREATED INTRAVESICALLY BY RADIUM. CASES IN WHICH TUMOR HAS BEEN REMOVED FROM BLADDER 1916 TO 1920, INCLUSIVE

Case	Age	Sex	Evidence of carcinoma		Extent	Induration	Urinary frequency D.	Urinary frequency N.	Wgt. loss	Previous treatment	Radium—Dose—Method	Result
			Cytoscopy	Pathology								
I.C.A.G.	69	F.	Cauliflower, non-pedunculated, sloughy	Careinoma (Ewing)	Base 3 cm. in diameter over l. ureter	?	3–4	3–4	0	Fulguration twiee	100 mc. 8 hrs. Bladder tube	Bladder clean 4 yrs. 4 mos. Cystoscopy
E.J.S.	54	F.	Papillary, sloughy in part	Papilloma (Ewing)	All around bladder neck and trigone	Vaginal, 5 cm. in diameter	q. hr. 5–20		?	0	100 mc. 8 hrs. 2 bladder tubes. Repeated twiee at 3 mos. interval	Bladder clean 1 yr. Cystoscopy. Well (letter) 4 yrs.
L.M.	70	F.	Papillary red tumor of bladder base	Carcinoma (Ewing)	Multiple large one on trigone	Vaginal, small area	Frequent & pain		0	Fulgurated 2 years	200 mc. 7 hrs. 2 bladder tubes	Bladder clean 2 yrs. then reeurrence (rapid growth). Removed by radium 1 yr. Radium burn
J.A.H.	62	M.	Rapidly growing, flat, ulcerated	Carcinoma (Ewing)	Small, operable near ureter	0	2–3		0	Fulgurated once	180 mc. 6 hrs. 2 bladder tubes. Repeated in 4 mos.	Bladder clean 4 yrs. (cystoscopy). (Kidney no function on side corresponding to tumor)
H.F.R.	68	M.	Sloughy papillary tumor	Papillary careinoma (Ewing)	Extensive bladder neck	?	q. hr.	q. hr.	17 lb.	0	100 mc. 8 hrs. 2 bladder tubes. Repeated 6 mos. later for recurrenee	1st, bladder clean 3 mos.; 2d, bladder clean 1½ yrs. Well 2½ yrs. (letter)
A.T.V.W.	59	F.	Papillary tumor, some slough, left trigone	Papillary careinoma (Ewing)	2 × 2 cm.	?	2–3	2–3	0	0	100 mc. 6½ hrs., 2 bladder tubes. Repeated 6 mos. later	Bladder clean once (eystoscopy)
F.H.P.	63	M.	2 tumors, 1 necrotie, 1 red	0	Around bladder neck	0	q. 3. hr. 2.		0	0	70 mc. 4 hrs. 2 bladder tubes	Bladder clean 4 mos. (cystoscopy). Well 2 yrs. (letter)
G.	64	F.	Tumor, flat, ulcerating, r. lateral wall	Epidermoid careinoma (Ewing)	2 × 3 cm.	0	q. 2 hr.	q. 2 hr.	0	0	100 mc. 5 hrs. 2 bladder tubes. Base tubes (2 of 0.5)	No tumor 8 mos. later (cystoscopy). Radium burn

W.	50	F.	Small, ulcerating, flat, back of l. ureter	Epidermoid carcinoma (Ewing)	3 × 3 cm.	0	0	0	0	100 mc. 6 hrs. 2 bladder tubes	No tumor 8 mos. later (cystoscopy)
H.	50	M.	Red, smooth, rounded tumor near r. sphincter	Questionable if carcinoma	3 × 3 × 2 cm.	0	0	0	0	Base tubes (0.5) through cystoscope	No tumor 1 yr. later (cystoscopy)
S.	53	M.	Multiple, sloughy, around bladder neck	Carcinoma (?) (Ewing)	Multiple, largest 1 × 1 ½ × 3 cm.	0	?	0	0	100 mc. 5 hrs. 2 ½ bladder tubes	No tumor 2 mos. later (cystoscopy)

Papilloma of Bladder

C.	60	M.	Bladder filled with grape-like masses, rec. post-op.	Papillary (Mandlebaum)	Bladder vault (?) full	0	?	0	Operation	2 tubes 50, 8 hrs.	Sl. tumor 3 yrs. 8 mos. later Treated. No. tumor 3 mos. later
Z.	42	F.	Multiple, red tumors around sphincter	Papillary (Ewing)	Multiple one 3 × 3 cm.	0	0	0	Fulguration	100 mc. 8 hrs. 1 bladder tube	Recurrence 3 yrs. later. Treated. No tumor 3 mos. later. Died hemorrhage
R.	63	F.	Multiple, red papilloma trigone	Papillary (Ewing)	5 × 5 × 4 cm.	0	0	0	0	90 mc. 7 hrs. 2 bladder tubes	Reported no papilloma 1 yr. later (cystoscopy)
O.D.	74	F.	Red, papillary growth behind l. ureter	0	5 × 5 × 5 cm.		0	0	0	100 mc. 8 hrs. 2 bladder tubes. Subsequent fulguration	No tumor 9 mos. later (cystoscopy)

operative risk. I opened his bladder and found a tumor on the right anterior wall, solid, of the size of a hen's egg. It had grown through the bladder wall and was adherent to the symphysis. We did not cut into the tumor for a specimen, but scraped off a slight portion of the surface which showed on examination mucus and pus. There was no doubt, however, of the clinical diagnosis of "carcinoma." This was the largest carcinoma that we had attempted to remove. We filled the tumor as accurately as possible with radium tubes of 0.2 cm., two to a cubic centimeter., leaving these in place. The bladder was drained for a long time because I feared the sloughy results from the radium absorption of the tumor. The patient's recovery was uneventful, barring the fact that he had a persistent suprapubic sinus. Three months after my first operation I cut out the bladder sinus and sewed up the bladder. During this operation I searched with my finger the site of the old tumor, and could find nothing abnormal, barring a slight irregularity about 1 cm. square in the surface of the mucous membrane of the bladder. He was last cystoscoped in February, 1921 and his bladder, while slightly hyperemic over the site of the tumor from the effects of the radium, showed no tumor. He is in the best of health, and has no symptoms except that he gets up once or twice at night to urinate.

Tables showing the results in both intravesical and suprapubic methods are appended to this article.

Intravesical. We have removed the carcinoma from the bladder in 11 cases by the intravesical application of radium. The longest case has gone four years and four months with the bladder clean of tumor and proved by cystoscopy.

Suprapubic. To January, 1921, we have operated upon 29 cases of carcinoma of the bladder. There were no deaths directly after operation, although one died seven weeks post-operation, and one two months post-operation. Some of these patients showed carcinoma so extensive that no radium treatment was attempted. In 10 of the 29 cases the carcinoma was removed from the bladder, the longest case having gone twenty months after operation with a bladder clean of tumor. Five of the cases have not been cystoscoped post-operation. The remaining 14 are dead or doing badly, and 1 has not been traced since he left the hospital. There has been but one implantation of tumor in the operative wound. This was in a case operated upon before he came to us—so we can divide the responsibility for it.

Examination of the chart will show how very extensive and inoperable all the tumors were if we exclude cystectomy. I have never seen any operative statistics that compare at all with those of the above table.

XVI

RADIUM THERAPY OF TERATOID TUMORS OF THE TESTICLE[1]

BENJAMIN S. BARRINGER, M.D. AND
ARCHIE L. DEAN, JR., M.D.

The purpose of this paper is to indicate a new conception of the therapy of teratoid tumors of the testicle.

Some years ago the late Dr. Janeway was able in several instances to destroy very large metastatic growths secondary to teratoma of the testicle. This was done by means of a "radium pack." The dose of radium for such a pack is 12,000 mc. hrs. placed over a tumor mass at a distance of 6 cm. from the skin, the filtration being 2 mm. of lead.

The following history illustrates the extraordinary effect of radium in one of these cases:

CASE I. Age, thirty-six years. First seen Oct. 23, 1916.

In 1906, right and left epididymitis.

In 1915, right testicle became sore, very large but not sensitive. Patient lost 15 lbs. in three months. Wassermann reported negative. Physical examination showed right testicle site of irregular semi-elastic tumor. There was a large mass, manifestly malignant, filling the right side of pelvis and protruding from right abdominal wall. A radium pack was applied to this mass. Two weeks later Dr. Keyes removed the tumor of the testicle and cord up to the internal abdominal ring. Pathological examination (Ewing) showed teratoma. Two weeks later (and four weeks after the radium application) the abdominal mass could no longer be felt.

On March 22, 1920 (three years and five months after first seen) the patient reported by letter that he was entirely well.

There have been several cases as brilliant as this. During the past few years we have attempted to determine which testicular teratomas react to radium and what is the best way to use this agent.

[1] Read before the Section on Urology at the Seventy-second Annual Session of the American Medical Association, Boston, June, 1921. Reprinted from the *J. Am. M. Ass.*, Oct. 15, 1921, lxxvii, pp. 1237–1239.

PATHOLOGY

Ewing places the varieties of teratoid tumors of the testicle in three main classes:

1. Adult embryomas or teratomas constituting a relatively small group.
2. Embryoid, teratoid or mixed tumors, more frequently seen than the above.
3. Embryonal malignant tumors, the testicle tumors most often seen.

The tumors arise, with rare exception, from sex cells situated in the rete testis, and the teratoma may develop either toward the testicle and epididymis, involving both in a large tumor mass, or much more rarely, toward the epididymis, forming a typical tumor of the epididymis. We have seen two tumors of this variety.

METASTASES

"The intraperitoneal nodes at the celiac axis are often involved through the lymph channels of the spermatic veins, and an epigastric tumor is often the first sign of recurrence. This form is especially common with the highly malignant embryonal carcinomas. From this point there may be rapid progress upward so that mediastinal and even cervical tumors may divert attention and become the largest tumors in the body. Invasion of the spermatic and iliac veins, with continuous tumor growth extending as far as the heart has been observed both with chondrosarcoma and chorioma. Discontinuous metastases by way of the veins is most frequent and gives rise to tumors of lungs, liver, brain, kidney and stomach." (*Ewing.*)

DIAGNOSIS

Notwithstanding that the situation of testicular tumors is favorable to palpation and observation, the diagnosis very often is difficult. One of us vividly remembers doing an operation for hydrocele and noting at the time of operation that there was what we took to be inflammatory change in the epididymis. The patient left the hospital healed. He went to another hospital a month later where a teratoma testis was

removed. When the tumor is typical, the whole testicle is an irregular, hard mass in which no distinction between the testicle and epididymis can be made, and the main diagnosis is between teratoma and gumma. In a large number of cases

FIG. 39. Teratoma testis. The epididymus and cord are invaded; the testicle proper is practically free of tumor tissue.

of gumma of the testicle, seen at Bellevue Hospital in the service of Dr. Keyes, we do not remember one that did not give a positive Wassermann. On the other hand, we have seen only one patient who had syphilis and a teratoma testis, who gave a positive Wassermann. Therefore a positive Wasser-

mann points strongly against the diagnosis of testicular teratoma.

We have seen 2 cases where the teratoma grew atypically and involved the epididymis alone, giving a picture not unlike tuberculosis of the epididymis. In one of these cases

FIG. 40. Longitudinal section of gross specimen. Removed twelve days following radiation of 13,070 mc. hrs. applied externally in form of pack. The testis measures 14 cm. in circumference. It is firm, fibrous and elastic. Section shows smooth translucent tissue, divided by several bands like the septa of the organ, and there are several necrotic areas 1 to 2 cm. wide, sharply circumscribed. Some of these are yellow, others orange-colored. The tunica albuginea is thickened, but intact. The upper nodes of the cord are slightly enlarged.

the diagnosis of teratoma was made prior to operation because of the secondary tumor mass in the abdomen. The preoperative diagnosis of teratoma is very important: we have never seen a patient in whom the tumor was incised

either for the purpose of making a diagnosis or under a mistaken diagnosis—hydrocele, spermatocele, epididymitis, etc.—that did not succumb to a local recurrence of the tumor.

When the teratoma occurs in an undescended testicle the diagnosis is still more elusive.

INEFFICIENCY OF PRESENT OPERATIVE METHODS

Orchidectomy. In 19 postoperative recurrent cases seen at the Memorial Hospital, orchidectomy had been performed upon 18. There were 8 recurrences in the groin along the spermatic cord; 7 in the abdomen along the spermatic lymphatics and 4 in the lungs. In 6 cases more than one region had become involved.

RADICAL OPERATION

Hinman reports several cases in which he has done the more radical dissection, taking out the testicular tumor and dissecting the fascia around the spermatic vessels up as high as the kidney. In one of his cases there was a secondary tumor of one of the perispermatic lymph glands which was dissected out. This patient lived for some months after the operation, apparently well.

PRESENT TECHNIQUE AT MEMORIAL HOSPITAL

We treat early cases as follows:

A careful physical examination is made, including *x*-ray plates of the chest. When distant metastases and regional involvement are not found the case is classified as "primary operable." The patient is admitted to the hospital and the testicular tumor, spermatic cord and abdomen along the tract of the spermatic vessels treated with the radium pack.[1] The dose over the testis is usually 12,000 mc. hrs. at 6 cm. distance, the filtration being 2 mm. lead. The same dose is considered sufficient for the other regions. The patient is now permitted to go to his home, but he returns for examination once a week.

We have found that the rapidly growing, cellular and more malignant embryonal types of these tumors are much

[1] FAILLA, G. Radium technique at the Memorial Hospital, New York *Arch. Radiol. & Electroth.*, June, 1920, xxv, 3.

more sensitive to the action of radium than those tumors in which adult tissue predominates. Therefore when the tumor rapidly reduces after radiation we know that we have to deal with a tumor in which embryonal tissue predominates. In such tumors it is our custom to delay operation for a number of weeks and even months so as to get the maximum effect of the radiation. In tumors which do not decrease in size after radiation we operate in from three to six weeks after the application of the pack. The technique of operation is as follows:

A curved abdominal incision is made beginning at the external abdominal ring, and sweeping outward and upward toward the kidney. The spermatic vessels are exposed, the vas is cut and the tissue on either side of the spermatic vessels (to the distance of about 1 cm.) is bluntly dissected upward as high as the renal vessels. This mass of tissue embodies the lymphatic vessels and glands around the spermatic vessels. All this dissection is extraperitoneal and during this time the testicle is still lying in its bed. Handling the testicle before its vessels and lymphatics are cut tends, we believe, to squeeze tumor cells into the general circulation.

If there are any glandular metastases, these are dissected out and tubes of screened radium (silver 0.5 mc. and rubber 2 mm.) are placed in its bed, using 200 mc. hrs. to each area 2 cm. in diameter. These tubes are later removed by attached strings. Finally the vessels are cut high up, the testicle is dissected out and removed and the wound sewed up. We have performed this operation eight times. We have had no postoperative deaths, and do not believe it to be a serious operation if infection does not occur. From three to six weeks after the wound is healed, radium packs are again applied over the length of the scar.

RESULTS

Of the 36 cases of teratoma testis treated at the Memorial Hospital during the past four years, there were:

1. Three cases classified as "primary operable," that is, 3 cases which were seen before operative procedure had been undertaken, and which at the time of admission showed by physical examination neither such local extension nor

metastatic involvement as would prevent complete operative removal of the tumor process. Of these cases, but 1 is living three months after first seen; 1 is dead and 1 untraced.

2. Eight cases classified as "primary inoperable." These included patients who had never been operated upon, but who presented at the time of admission the physical signs of metastases, so that operative procedure could offer no hope of complete removal of the disease.

In one of these the diagnosis of teratoma was made prior to operation because of the secondary tumor mass in the abdomen.

Of these, 3 are living, two, three and forty-one months after first seen; 3 are dead and 2 untraced.

3. Nineteen cases of "postoperative recurrent teratoma." These patients had received surgical treatment elsewhere and had been referred to the Memorial Hospital at various intervals after the appearance of recurrences. Of these, 5 are living, seventeen, twenty-eight, eighteen, twelve and three months after first seen; 8 are dead and 6 untraced.

4. Six cases classified as "for prophylatic radiation." These patients had been referred after operation elsewhere, but before recurrences had been observed. Of these 2 are living, two and nine months after first seen; 2 are dead and 2 untraced.

One of the primary operable cases radiated before and after operation, as outlined above, died of recurrences some months after operation. The teratoma in this case was of the adult type.

These statistics emphasize the extreme malignancy of teratoma testis. We believe, however, that radium is a very valuable adjunct to operation in dealing with this disease. The type most often seen and most malignant, the embryonal, is the most sensitive to destruction by radium.

XVII

EPITHELIOMA OF THE PENIS

Benjamin S. Barringer, m.d., and
Archie L. Dean, Jr., m.d.

The purpose of this paper is to add to the literature a statistical study of 36 cases of epithelioma of the penis, seen and treated at the Memorial Hospital during the past four years.

The age of the patients at the time of onset ranged between fifteen and seventy-four years, with the decades divided as follows:

0–10 years	0 cases
10–20 years	2.7 per cent cases
20–30 years	2.7 per cent cases
30–40 years	19.0 per cent cases
40–50 years	19.0 per cent cases
50–60 years	30.0 per cent cases
60–70 years	19.0 per cent cases
70–80 years	5.0 per cent cases

Eighty-one per cent had been married, 19 per cent were single. Every type of occupation was represented.

As to race, 13.5 per cent were Negroes, 86.5 per cent were white. No Jews appear in this series. The United States was claimed as the birthplace by 48 per cent, Ireland by 27 per cent, Italy by 11 per cent, the West Indies by 6 per cent, Scotland and Germany by 3 per cent, respectively.

Regarding previous venereal diseases, all disease was denied, and no positive signs were obtained in 39.5 per cent. Gonorrhea was admitted by 19 per cent, syphilis by 5 per cent, gonorrhea and syphilis by 5 per cent, and chancroid by 3 per cent. All disease was denied, but positive signs of syphilis were present in 8 per cent, and in 16 per cent no record respecting this question was found.

CAUSE

The causes ascribed by the patients themselves were of some interest. Trauma was given as the exciting cause by 8 per cent. Of these 2 cases, or 5 per cent, might merit consideration, namely, "adhesion to the condom" and "injury during coitus." The third, "rubbing against the clothing," might well have occurred subsequent to the onset of the disease. One patient, or 3 per cent, traced his tumor to a congenitally retracted penis for the relief of which three operations had been performed.

Five per cent noticed a development from a venereal sore. Eleven said "tight foreskin," and the same number believed the epithelioma resulted from their circumcision. Fifty-seven per cent knew of no contributing cause.

The examining physician attributed the cause to phimosis in 76 per cent; to syphilis, 13 per cent; no cause apparent, 5 per cent; no record, 5 per cent.

The cases possibly associated with syphilis consisted of 4 instances in which typical gummata appeared on the shaft of the penis in patients obviously luetic. When the lesions failed to heal in spite of thorough specific treatment, biopsy revealed carcinoma. In another patient, the chancre occurred on the glans beneath a tight prepuce. Soon after the administration of the first dose of arsphenamine, paraphimosis appeared, and circumcision uncovered a neoplasm.

In 3 cases, or 8 per cent, beneath a tight prepuce there was a well-defined area of leucoplacia, surmounting, and in each instance surrounded by, carcinomatous infiltration. The leucoplacial patch was white, glazed and horny, and the patients stated that from time to time scaling of the surface took place. According to the histories, the leucoplacia was observed several years before any hardness or ulceration suggested malignancy.

The close relationship between phimosis and carcinoma of the penis has long been recognized. It is extremely rare to encounter this lesion in Hebrews. Another example of the prophylactic efficiency of circumcision is found in the report of Sutherland in which a statistical study is made concerning the prevalence of malignant disease at the Mayo Hospital, Lahore, India.

"A glance at the result of the race analysis shows a more or less equal prevalence of malignant disease among the two peoples (Hindus and Mohammedans) with one important exception. This exception is in the case of carcinoma, where the Hindu admissions exceed the Mohammedan by 80, a difference almost entirely due to 72 cases of epithelioma of the penis among Hindus, an affection from which Mohammedans (who practice circumcision) rarely suffer" (*Arch. Middlesex Hosp.*, Vol. iii).

When, as the result of a prepuce difficult or impossible to retract, there is added the irritation of retained inspissated smegma, the circumstances are ideal for the development of penis cancer.

SYMPTOMS

The first symptom in 54 per cent of the cases was a small sore on the penis; 14 per cent felt a lump beneath a tight prepuce, 8 per cent first noticed a wart; 8 per cent that their circumcision did not heal, and 5 per cent were circumcised, an epithelioma being revealed. Evidently in these last two divisions, comprising 13 per cent, the tumor was present before operation. Three per cent first noticed a progressive enlargement of both penis and scrotum; 3 per cent, a Negro, saw a reddish discoloration of the skin. One of the leucoplacia cases (3 per cent) was first aware of a "white scab on the glans penis, which would scale off, and break down, and then heal." Soon the cycle would be repeated.

Thus it may be noted that in practically all of the cases, even though phimosis and chronic balanitis had been present for years, a condition appeared which was recognized by all as something decidedly different, though its nature was not appreciated. Moreover, in every case, even though a condition of irritation had been present for a long time, the area of true epithelioma was quite small when it was first noticed.

After the appearance of the new growth, certain events followed which in 81 per cent of the cases consisted in a progressive enlargement of the lesion. Other symptoms in the order of their frequency were the following: Pain, 58 per cent (aching, 22 per cent, stinging, 14 per cent, sharp and burning, 11 per cent, itching, 11 per cent); purulent dis-

charge, 8 per cent; paraphimosis, 5 per cent; bleeding, 5 per cent; obstruction to urethra, 5 per cent; frequency of urination, 3 per cent. Occasionally the same patient had a combination of these symptoms but the usual story was that a sore appeared which steadily increased in size, and soon became painful.

INITIAL TREATMENT

Since the possibilities of relief or cure of carcinoma depend so much upon early treatment, a record was kept of this factor. Eight per cent of the patients sought advice immediately. In 22 per cent of the cases there was either no record, or the patients had forgotten. In the remaining, or 70 per cent, a delay occurred of between two weeks and nine years, five months; or an average of 14 months, plus, before treatment was sought.

The therapy employed after advice had been obtained was as follows: "Washes, salves, dusting powders, local applications," 39 per cent; radical amputation, 14 per cent; local amputation, 8 per cent; radium and *x*-rays, 8 per cent; antiluetic, 8 per cent; "caustic, electric treatments, cautery, fulguration, circumcision," 3 per cent each, or 18 per cent: 16 per cent were immediately referred to the Memorial Hospital.

While these various lines of therapy were being pursued, an average of forty-one weeks, or ten months per patient, elapsed. This was in addition to the fourteen months' delay for which the patients were responsible. There was therefore an average elapsed period of twenty-four months from the beginning of the disease until the patient came to the Memorial Hospital.

EXAMINATION

In spite of these delays, our general physical examinations showed 84 per cent of patients to be in good condition, 8 per cent to be classified as fair, and 8 per cent poor.

There had been no loss of weight in 64 per cent of the cases, and amounts varying between trifling to 40 lbs. in a year were reported in the remaining 36 per cent.

Likewise, 64 per cent of the patients were unable to work, and 36 per cent were following their usual occupations.

Considering the type of lesion, 56 per cent were indurated ulcers, 36 per cent were papillary, and 8 per cent were not recorded.

In respect to size, 10 were 5 sq. cm. or less, (27 per cent); 3 were 10 to 15 sq. cm. (8 per cent); 8 were 15 to 20 sq. cm. (22 per cent); 13 were 20 sq. cm. plus (36 per cent); not recorded 2 minus (5 per cent). The development of some of these tumors was remarkable. Perhaps the largest was described as the "size of a baseball," involving the distal three-fourths of the penis; it covered 40 sq. cm.

Two interesting considerations were mentioned by Barney, namely, the location of the lesion and its point of origin. In our series it was quite impossible to obtain these data for classification. The reason was that of the 36 cases considered, 22 different locations were described, and 17 points of origin were mentioned. In general, however, most of the lesions were first observed at some point on the glans penis, and increase in size was associated with involvement of contiguous parts of the organ.

INGUINAL ADENOPATHY

In 12 (33 per cent) the inguinal nodes were thought infectious; in 11 (30 per cent) carcinomatous; no enlargement, 2 (5 per cent); questionable, 3 (8 per cent); no record, 3 (8 per cent).

PATHOLOGY

Before undertaking the consideration of the therapy of this series, it might be well to consider the pathology involved, since it must be the basis of our treatment.

Two clinical types of carcinoma of the penis are described, namely, the papillary or cauliflower, and the indurated ulcer. The former is usually mentioned as being the more common, but in this series the latter type predominated to the degree of 60 per cent over 40 per cent. The most frequent site of origin is the glans, and next in frequency is the mucosa of the prepuce.

The earliest signs of the two are different. The papillary type begins in a group of wart-like excrescences. These increase in number, gradually spreading over a larger

surface, and at the same time becoming more elongated. Parts of the tumor break down, forming areas of ulceration, and occasionally bleeding may be an obtrusive symptom. This type has a tendency to remain localized. The dense protective tunic of the glans penis is a firm barrier to the extension of the disease. Once this has been pierced, and the loose cavernous tissue involved, the progress of the disease is much more rapid.

The infiltrating ulcer first appears as a superficial pink pimple, with a tiny ulcerating crater. The area of ulceration increases in size, and after a time infiltration advances, and finally, as with the papillary type, the tunic covering the glans penis is penetrated, and progress from thence on is more rapid.

Metastasis probably occurs by embolism through the lymph channels, and permeation along lymph vessels represents a later stage. The metastases may be either by way of deep lymphatics which accompany the dorsal artery and vein, and join pelvic nodes, or through superficial vessels to the inguinal nodes. This latter group of lymph-nodes usually (80 per cent) shows enlargement and increased density, but is not necessarily involved with carcinoma. The necrosis and secondary infection of the penis lesion is an adequate cause in most instances for extensive regional adenopathy. Sometimes in the earlier or less infected cases the inguinal enlargement is unilateral and corresponds with the side of the penis affected with the epithelioma.

Diagnosing the presence or absence of carcinoma in enlarged inguinal nodes is extremely difficult and often impossible, and many times our type of therapy is based almost entirely upon the opinion respecting this factor. The status of the deeper pelvic nodes can rarely be learned, but fortunately this is of lesser importance, because the inguinal metastases occur relatively much earlier in most cases. It has appeared noteworthy in this series that metastasis in general has occurred relatively rather late in the disease. In fact, in several instances the organ was almost entirely destroyed without any microscopic evidence of malignant involvement of the removed inguinal nodes. The papillary type of tumor seems to be the less dangerous in this respect.

TREATMENT

1. For the papillary carcinoma without induration of its base and without penetration of the tunic of the glans penis, surface radiation with radium is apparently the method of choice.

2. If there is induration and some penetration of the tunic of the glans, and but slight extension along the penis, implanted radium *may* cure.

3. If there is extensive involvement of the glans penis, local amputation, 2.5 cm. beyond the growth is indicated.

INGUINAL LYMPH-NODES

Most of the lymphatics of the penis drain into the lymph-nodes of the inguinal region, and in early cases of carcinoma of the penis, a careful and complete bilateral block dissection of the inguinal nodes ought theoretically to limit the extension of the carcinoma. The problem is, however, not as simple as this. The following are various phases of the question of what to do with these nodes. Barney says: "Glandular enlargement occurs in 75 per cent; 40 per cent are hypertrophic, and 60 per cent carcinomatous." In other words, in 45 out of every 100 cases of carcinoma of the penis, the inguinal nodes are carcinomatous. Yet in 74 primary cases, amputation alone was performed in 46, and groin dissection in but 16. The totally cured cases were 27, or 36.5 per cent, probably indicating that 45 per cent is too high an estimate of inguinal involvement.

Broders finds that 100 per cent of patients with metastases who had lesions of the penis obtained poor results, 63 per cent of patients without metastases obtained good results, and yet further down: "100 per cent of the patients in whom no inguinal lymph-nodes were removed obtained poor results." Others have said that if the lymph-nodes were carcinomatous dissection of them was bound to be incomplete, and would result in local recurrence at the site of the operation.

Streptococcic infection of the inguinal nodes is fairly common. A tight foreskin harboring a carcinoma is impossible to keep clean, and is the source of this infection. If, in addition to a streptococcic infection, the inguinal nodes are

carcinomatous, a combination is formed almost impossible to cope with. The infection has to be overcome before the nodes can be touched, and the only way to overcome this is to deal first with the source of infection in the penis. There is a certain mortality attached to the dissection of the inguinal nodes. We have lost 2 cases in old persons (in 1 of which the nodes were not carcinomatous) from infection of the wound.

Quick (Conservative treatment of cervical lymphatics in intraoral carcinoma, *J. Am. M. Ass.*, August 6, 1921) respecting the treatment of intraoral carcinoma, similar in many ways to penile carcinoma, says that many unnecessary operations will be performed if a blanket rule of block dissection be followed in all cases, and the operative mortality will certainly rise. He deals with the nodes of the neck conservatively, only dissecting them out when they become palpable, then burying radium tubes along the chains of cut lymphatics.

Ewing's work is the basis of Quick's conclusions. The following is therefore the procedure which, in the light of our present knowledge, is the best in dealing with the inguinal lymphatics:

1. If no nodes are palpable, the groins are given *x*-radiation and watched.

2. If nodes are palpable, but thought to be only infectious, the primary focus in the penis is treated, and the groins radiated and watched.

3. If the nodes are carcinomatous, and this diagnosis is hard to make, they are radiated, and then bilateral dissection is done with radium buried along the lymph channels, either in the form of bare tubes or screened radium, the most important place to radiate being the lymph channels around the saphenous opening.

4. If the nodes are thought to be infected and carcinomatous, the lesion on the penis is dealt with, and the source of the infection cleared up before the inguinal nodes are touched.

5. If the nodes are dissected out, the wound is partly sutured, and Dakin tubes left in place, so that the Dakin irrigation may be employed until granulation occurs.

RESULTS

These are best shown by dividing our cases into four classes:

1. Those in which the inguinal nodes were not thought to be involved, and were not treated by radium or *x*-rays; 7 cases, in 2 of which the disease was proved by biopsy, and 5, no biopsy. Radium application to the penis was the only treatment in 6 cases, and radium and amputation of the penis, in 1 case.

Of these 7, 1 died, one week after amputation of the penis, and 1, three months after radium treatment, cause unknown. One disappeared after one treatment, 1 was lost track of, and 1 is under treatment. There were but 2 which did well; 1 free from disease after radium for twenty-seven months, and 1 after radium and amputation for thirty-nine months. There was no biopsy in either of these cases, and both were small lesions.

2. Carcinoma of the penis, in which the inguinal nodes were thought not to be involved, but were treated by radium or *x*-rays, 12 cases.

Both radium treatment and amputation of penis were employed in 8 cases; radium alone in 3 cases; *x*-rays in 1 case.

One is dead, twelve months post-amputation, from senility; 3 are under treatment, not benefited, or result not known.

Five are disease-free, six to twelve months. One was treated by radium alone, and 4 by radium and amputation. There was a biopsy in 4; 3 of these were malignant, and 1 was epithelial papilloma. The size of the tumors in this group varied from 4 to 40 sq. cm.

Three are disease-free, twelve to twenty-four months. There was biopsy in all, and the tumors measured from 3.5 to 30 sq. cm.

3. Carcinoma of penis, in which inguinal nodes were thought to be malignant, but were only treated by radium or *x*-rays, 8 cases.

The mortality figures here rise. But 1 case, a carcinoma in which the entire glans was involved (20 sq. cm. plus) has gone forty-three months without recurrence. Four are dead,

1 died a week after operation of uremia. The others lived three months, ten months and thirty-eight months, respectively, after treatment. Three are no better, or are under treatment.

4. Carcinoma of penis, in which the inguinal nodes were thought to be involved, and were dissected out, 8 cases; 3 of these are well, twelve to twenty-four months, 2 are well, twenty-four to thirty-six months, and 3 pathologically showed metastases in inguinal nodes.

The size of the primary tumor in these was, in sq. cm., 3.5, 18, 20, 25, respectively, and 1 not known.

So, out of 36 cases, 16 are, as far as can be seen, disease-free: 5, six to twelve months, 6, twelve to twenty-four months, 3, twenty-four to thirty-six months, 2, thirty-six to forty-eight months.

We can say nothing of the cure of these cases, as enough time for this has not elapsed.

SUMMARY

1. Both papillary and infiltrating carcinoma of the penis may be removed by radium, if the tunic covering the glans penis has not been penetrated.

2. After penetration of the tunic, surgical removal 2.5 cm. proximal to the growth is indicated.

3. Metastasis probably occurs by embolism through the lymph channels, and is usually noted earliest in the inguinal nodes.

4. From existing statistics, it is probable that inguinal involvement by carcinoma is relatively late, and occurs in rather less than 40 per cent of cases.

5. We believe that the best results are obtained by conservative treatment of the inguinal nodes, with routine *x*-ray treatment of all cases, withholding surgical removal until they are believed to be definitely carcinomatous. Then, after removal, the lymph channels should be radiated.

6. No surgery should be done on the inguinal nodes, if they are the site of a pyogenic infection. The source of such infection, the penis, should first be dealt with.

TABLE I

Case number	Type	Size, sq. cm.	Pathology	Estimate of inguinal nodes	Treatment of penis	Treatment of inguinal nodes	Results	Died
29956	Papillary	30.0	Epidermoid carcinoma	Inflammatory hyperplasia	1. Radium 2. Amputation	*X*-ray	No disease, 16 months	
29662	Indurated ulcer	0.5	No biopsy	No adenopathy	Radium	*X*-ray	No disease, 12 months	
3	Indurated ulcer	3.0	No biopsy	No record	Radium	Not treated	No disease, 27 months	
30422	Papillary	30.0	Epithelioma	Inflammatory hyperplasia	1. Radium 2. Amputation	*X*-ray	No disease, 8 months	
5	Indurated ulcer	4.0	No biopsy	Questionable	Radium	Not treated		3 months; cause unknown
6	Indurated ulcer	30.0	Infiltrating epidermoid carcinoma	No record	Radium	Not treated	Seen once; unknown	
26739	Indurated ulcer	3.0	No biopsy	No record	1. Radium 2. Amputation	Not treated	No disease, 39 months	
28736	Papillary	40.0	Epithelial papilloma	Inflammatory hyperplasia	1. Radium 2. Amputation	*X*-ray	No disease, 12 months	
30190	Papillary	24.0	Infiltrating squamous carcinoma	Inflammatory hyperplasia	1. Radium 2. Amputation	*X*-ray		12 months; senility
10	Papillary	25.0	Squamous carcinoma	Metastatic carcinoma	1. Amputation 2. *X*-ray	1. Removal 2. *X*-ray	No disease, 14 months	
28653	Papillary	15.0	Epithelial papilloma	Epithelial papilloma	1. Radium 2. Amputation	1. *X*-ray 2. Removal		21 days; tuberculosis; pneumonia
29192	Indurated ulcer	20.0	Epidermoid carcinoma	Inflammatory hyperplasia	1. Radium 2. Amputation	1. *X*-ray 2. Removal	No disease, 21 months	
28617	Indurated ulcer	4.0	Squamous carcinoma	Metastatic carcinoma	1. Radium 2. Amputation	1. Radium 2. Removal		8 days; sepsis
29852	Indurated ulcer	4.0	Epidermoid carcinoma	Inflammatory hyperplasia	Radium	*X*-ray	No disease, 13 months	
28480	Papillary	12.5	Squamous carcinoma	Inflammatory hyperplasia	1. Radium 2. Amputation	1. *X*-ray 2. Radium	No disease, 8 months	
16	Not known	Not known	Epithelioma	Epithelioma	1. Amputation 2. *X*-ray	1. Removal 2. *X*-ray	No disease, 35 months	
29644	Papillary	3.5	Papillary epithelioma	Metastatic carcinoma	1. *X*-ray 2. Amputation	1. *X*-ray 2. Removal	No disease, 31 months	
18	Indurated ulcer	2.0	No biopsy	No adenopathy	Radium	Not treated	Improved; under treatment	

31274J'	Indurated ulcer	3.5	Infiltrating squamous carcinoma	Inflammatory hyperplasia	1. Radium 2. Amputation	*X*-ray	No disease, 18 months	
31202	Indurated ulcer	40.0	Infiltrating epidermoid carcinoma	Metastatic carcinoma	1. Amputation 2. *X*-ray	1, *X*-ray. 2. Radium. 3. Removal		Dying of recurrence
29261	Indurated ulcer	20.0	Squamous carcinoma	Inflammatory hyperplasia	1. Amputation 2. Radium	*X*-ray	Not known	
28529	Indurated ulcer	40.0	Epidermoid carcinoma	Inflammatory hyperplasia	1. Radium 2. Amputation	Not treated		8 days; uremia
23	Papillary	21.0	Epithelial papilloma	Inflammatory hyperplasia	Radium	*X*-ray	Refused operation; only temporary improvement	
28325	Papillary	18.0	Specimen lost	Metastatic carcinoma	1. Radium 2. Amputation	1 *X*-ray 2. Removal 3. *X*-ray	No disease, 22 months	
30628	Papillary	11.0	Epidermoid carcinoma	Inflammatory hyperplasia	1. Radium 2. Amputation	*X*-ray	No disease, 7 months	
30553	Indurated ulcer	40.0	Squamous carcinoma	Metastatic carcinoma	Radium	*X*-ray	Under treatment	
27	Not known	20.0	Carcinoma (B.H.)	Metastatic carcinoma	1. Amputation. 2. *X*-ray	*X*-ray	No disease, 43 months	
31280	Indurated ulcer	19.0	No biopsy	Metastatic carcinoma	Radium	*X*-ray	Under treatment	
29	Not known	Not known	Carcinoma	Metastatic carcinoma	1. Amputation. 2. *X*-ray	*X*-ray	Not known	
30	Papillary	20.0	Carcinoma (B.H.)	Metastatic carcinoma	1. Amputation. 2. *X*-ray	1. Removal. 2. *X*-ray	Not known	
31	Indurated ulcer	28.0	Epidermoid carcinoma	No record	Radium	Not treated	Refused operation	Not known
28259	Papillary	30.0	Squamous carcinoma	Inflammatory hyperplasia	*X*-ray	Radium pack	Not benefited; refused further treatment	Dead
27266	Indurated ulcer	20.0	No biopsy	Metastatic carcinoma	Radium	*X*-ray	Extension into bladder	8 days after cystotomy
34	Indurated ulcer	4.0	No biopsy	Metastatic carcinoma	Radium	*X*-ray		38 months
28567	Indurated ulcer	30.0	Squamous carcinoma	Metastatic carcinoma	1. Radium. 2. Dorsal slit	Radium pack		3 months uremia
26597	Indurated ulcer	20.0	No biopsy	Metastatic carcinoma	Radium	Radium		10 months

XVIII

THE PRESENT FIELD FOR THE USE OF THE X-RAYS AND RADIUM IN THE TREATMENT OF MALIGNANT NEOPLASMS[1]

WILLIAM S. STONE, M.D.

Roentgen rays and radium in the treatment of malignant tumors are still accepted reluctantly by the surgeon, except as palliative agents in the advanced stages of the disease. Their application before the patient is in an incurable stage appears to be an insufficiently tested method. In the case of *x*-rays it is particularly so, for, before the recent advent of the high-voltage machine, *x*-ray therapy had become so overshadowed by the results of radium that it had lost somewhat of its early reputation.

It seems, therefore, to be an opportune time to review this work, as it has been presented to the writer during a service of seven years at the Memorial Hospital. During this period more than 10,000 cases of neoplastic disease have been under his observation, to the majority of which *x*-rays or radium have been applied. We feel that we have now arrived at a position in this work from which we may discuss *the surviving old, the established new,* and *the still experimental.*

As to the *surviving old,* the operation no longer maintains its former position of being the only method of treating cancer in the curable stage. It is no longer in many fields the method of choice. There still remain, however, numerous fields in which our enthusiasm for the physical agents must not allow the postponement of the operation to lessen or take away its chances of success. In all the well-advanced cases, and in those designated as being in the borderland of operability, in which formerly a radical operation was attended by a high primary mortality and a low percentage

[1] Read at the Seventh Annual Meeting of The American Radium Society, St. Louis, Mo., May 22–23, 1922. Reprinted from the *Am. J. Roentgenol.*, Aug., 1922, ix, 502–507.

of cures, the surgeon's responsibility is not fulfilled until all the aid has been enlisted which *x*-rays and radium can supply. In fact, there are few, if any, early cases of malignant tumors in which these agents do not merit consideration, if only as an adjunct to the operation. In other words, the surgeon's position as a technician has been made easier, but from the viewpoint of diagnosis and proper selection of cases, his reponsibility has become greater. Even in diagnosis, the therapeutic test of irradiation will often render an exploratory operation unnecessary. Instead, therefore, of being supplanted by these agents, the field of applicability of the operation has been limited strictly to the earliest stages, by which also we may hope to define more accurately its curative value.

Of the *established new*, we now have numerous facts relating to the conditions upon which the effects of irradiation depend. While the early observations have been confirmed that tumor cells, in general, respond more promptly to the action of the *x*-ray and radium than the normal tissues, such wide variations are shown among the different types of tumors, even between tumors of the same type in different parts of the body, that we can hardly appreciate the basis for speaking of a carcinoma or a sarcoma dose. Just as wide variations also occur among the sarcomas as among the carcinomas.

The effects of irradiation depend upon the size, extent and condition of the tumor. The size, however, is of less importance than with the operation, some of the bulkiest of abdominal tumors, for example, disappearing within a few weeks. The extent of the tumor is also of less importance, but an extension to a neighboring bone, unless the tumor is of the most responsive type, will seriously interfere with the result.

The condition of the tumor and its neighboring tissues, next to its type, determines the success or failure of irradiation more than any other factor. Infected tumors respond unfavorably, and a syphilitic base, in a lesion of the tongue, for example, invariably hinders the progress of the regression. A tumor also with altered nutrition, in which the general condition of the patient may still be apparently good, may

soon become so necrotic from the irradiation that the terminal period of the disease is prematurely initiated. The fear of toxicity, however, from the absorption after irradiation of the products of disintegration in a normally nourished tumor has been, I believe, somewhat exaggerated in the literature. Fibrosis resulting from an operation or a previous irradiation makes a tumor less responsive. The greater effects of these agents upon tumors and normal tissues which have not been previously irradiated is universally accepted by all observers. The existence of normal neighboring tissues and their preservation by the avoidance of overdosage constitute an important factor in the process of cure. The killing of the cancer cell is only one of the essentials, to which must be added a proper amount of inflammatory reaction on the part of the stroma of the tumor and normal tissues. For this reason, also, a poor condition of the general health, altering the nutrition of the tissues about the tumor, makes conditions which are unfavorable for regression of the tumor.

The general health of the patient must be considered, also, because of the toxemia which necessarily results from the application of these agents—a subject which deserves more consideration, especially in the case of elderly people, than it has hitherto received. The effect of these agents upon the blood must also demand our attention. It is not improbable that the cell count may become an aid in determining the intervals between treatments. In observing the general condition of the health, it is necessary to distinguish between a condition resulting from hemorrhage or toxicity from a necrotic tumor, and the cachexia from the generalization of the growth. In the latter condition, any treatment is contraindicated, but in the other conditions a stoppage of the hemorrhage or the removal of a necrotic focus may enable irradiation subsequently to produce satisfactory results.

Much confusion exists regarding the relative merits of *x*-rays and radium, but so far as we are able to judge clinically, the effects of *x*-rays and the gamma rays of radium are the same. With a supply of 4 gm. of radium, however, we have been able to obtain more marked effects upon deeply situated tumors than we have from the use of the *x*-ray machines delivering not over 100,000 volts. The effects of

each depend upon the power of absorption the tissues possess for rays of certain wave-length. Some of the gamma rays, we know, are of such short wave-length that they penetrate the tissues without being absorbed, and without, therefore, producing therapeutic effects. We hope, then, to obtain from the transformer producing a higher voltage a quantity of *x*-rays of sufficiently short wave-length to make this agent an efficient substitute for radium in cases in which deep effects are required. It will be an error, however, to undervalue the therapeutic effects that have already been obtained by the use of the lower voltage machines. Numerous cases do not require rays of shorter wave-length than these can produce, and with a technique in which distance, filtration and time are increased materially, we await improved results with the old machines.

A review of the material from which these general facts were obtained enables us to present numerous clinical fields in which, although the response to irradiation varies widely, the results indicate that *x*-rays and radium have a specific field of applicability.

Lymphosarcoma, metastatic teratoid tumors of the testicle, certain embryonal tumors of the kidney in children and a type of bone sarcoma recently described by Ewing as endothelial myeloma, represent types of neoplasm which promptly respond either to the gamma rays of radium or *x*-rays after a single application. The unfortunate results of biopsy or operation in lymphosarcoma may be avoided by the therapeutic test in cases of a doubtful nature. The metastatic teratoid tumors of the testicle are even more responsive than lymphosarcoma, but we are not yet prepared to offer definite conclusions regarding the treatment of the primary tumor. For the present, we think it should be excised after a preliminary irradiation. We have observed only a few embryonal kidney tumors in children, but in each case the regression has been favorable. The endothelial myeloma may be best discussed with the other bone tumors, but the response to irradiation is so similar to lymphosarcoma that they are included in this group.

There are other tumors in which the response to these agents is often prompt, but the results vary. *Mixed tumors*

of the *parotid*, depending upon their individual structure, vary widely, but on account of the nerve palsy and deformity that so often follow the operation, a preliminary trial of irradiation should always be made.

The results in basal-cell epithelioma, or rodent ulcer, discovered by the pioneers in *x*-rays to be susceptible to that agent, have been so greatly improved by radium that operation is rarely indicated. Errors in diagnosis, however, are easily made, and the condition of the growth has been so often altered by unsuitable previous treatment that it may be wise to give a guarded prognosis. In lesions near the eye, in which ectropion so invariably follows the operation, the superiority of radium is well shown.

There is a large field of ulcerating growths of the skin and mucous membranes, in which, by the additional use of the beta rays and by implantation of radium into the tumor tissues, results have been achieved in many instances beyond those that have hitherto been accomplished by the knife or cautery. In this way, during the past three years, lesions of the lip, tongue, mouth, tonsil, larynx, etc., have been brought into a group in which the operation has been supplanted, practically, by the use of radium. This use of radium, however, is taking advantage to some extent of its caustic qualities, concerning the action of which there remains much to be investigated. In all these lesions, especially of the lip and tongue, the regional invasion of the lymph-nodes presents the most difficult part of the problem, for the solution of which a judicious combination of surgery and these agents is required. For the performance of this work considerable experience in their use, and radium in a suitable form, are necessary, so that the choice of procedure may depend upon the amount of experience in the use of these agents that the patient is able to command.

In uterine cancer, radium has achieved its most brilliant success as a curative agent, especially in lesions of the cervix, in which surgery has now a very limited field, if any, of applicability. The results of surgery, however, in early lesions of the uterine body are so good that, for the present, at least, operation after a preliminary use of radium appears to be the method of choice. A most conservative statement would be

that any uterine lesion requiring more than a simple hysterectomy for its cure should be treated by radium. Our experience with the *x*-ray does not justify our reliance upon this agent alone in the treatment of uterine cancer. Even in Germany, there have been only a few cases, I believe, in which radium has not been used in connection with *x*-rays.

The results in all the other growths of the mucous membranes fall short of those we have just discussed. There is little evidence of practical accomplishment in cancer of the esophagus and stomach. Our primary results in tumors of the bladder, because of the frequency of their papillary and non-infiltrating character, justify the expectation that these agents will have definite curative value. There is already no doubt of the palliative value of radium. There is also much evidence of its palliative value in cancer of the prostate, but specia care is needed in the selection of cases, because the treatment temporarily adds to the patient's discomfort, and the prolongation of life must, therefore, be sufficient to justify the attempt.

Cancer of the rectum has proved a more difficult problem than our first results led us to expect. The extreme sensitiveness of the normal mucosa makes it difficult to give a sufficient dosage, and in an annular growth a permanent stricture is practically impossible to prevent. Life in such instances may be prolonged, but it is usually at the expense of suffering. In any serious effort to cure this lesion by irradiation a preliminary colostomy is necessary. Annular lesions, to be suitable for radium treatment, must be practically of the same early type in which the operation is indicated. In lesions limited to part of the circumference of the rectal wall, surface irradiation combined with the implantation of radium in the growth, and followed subsequently by excision, has produced better results than could be obtained by the operation alone. Cessation of bleeding and pain in a few advanced lesions have been accomplished by the use of the gamma rays. It may be that *x*-rays will accomplish much better results.

There is little need of discussing the applicability of these agents to inoperable and recurrent lesions, except to direct attention to the abuses which the circumstances surrounding

the patients in these stages of the disease so often lead us to practice. It is surprising how long an interval will elapse before a patient with a recurrence is referred to a radiologist, whereas there is the same necessity of treatment in the early stage as there is in the case of the primary growth. Neither agent is applicable for the terminal period of the disease. It too often happens that, instead of receiving morphin and good nursing care, the patient is dragged about in the forlorn hope of being helped by *x*-ray or radium. Both the surgeon and the radiologist are responsible for these abuses. The surgeon, whose enthusiasm for the use of irradiation may begin only when he sees the opportunity of avoiding a disagreeable situation, too often emphasizes its value then, and the radiologist is able only to carry out what he knows to be a hopeless undertaking. The performance of an incomplete operation before the case is referred to a radiologist is fortunately becoming less frequent. In New York, we have seen this most frequently in the case of uterine cancer, in which the removal of the uterus materially lessens the value of irradiation. However, in the proper selection of cases, some of the most advanced growths have yielded to irradiation in a remarkable way. As with the primary tumor, success depends upon the type, size, extent and condition of the growth. Regarding metastases, the writer has been fortunate in observing favorable results following the application of the gamma rays of radium to bone metastases from mammary cancer. There appears to be more than an even chance of relieving pain, and in a few instances, the repair of the lesion, as shown in the roentgenograms, and a temporary restoration of the general health have justified our efforts.

Of the *still experimental*, it may fairly be said that all this work is experimental, because, even in the fields where much has been established there is much more awaiting both laboratory and clinical research. There are a few clinical problems, however, in which we are now especially interested.

The prophylactic use of irradiation before and after operation is, perhaps, one of the most important, and cancer of the breast, although much has already been established regarding the irradiation of this tumor in its advanced stage, presents a profitable field for the discussion of this

subject. Growths of these organs vary widely in their nature and in their response to irradiation. We have observed that a few primary tumors apparently disappear after the application of *x*-rays and radium. A partial regression has been observed in a large number, and after repeated applications they have shrunk to an inactive lump. We have also seen tumors inoperable because of their extent and fixation become transformed into tumors that were apparently operable. As our technique has improved, and radium has been implanted in the tumor tissues, much better results have been observed, so that a few cases, in which for special reasons the operation was contraindicated, we have trusted to irradiation alone. From such observations we must conclude to make use of these agents in conjunction with the operation during the early stages of the growth.

The postoperative application is becoming a routine procedure, and it is reasonable to believe that an increased number of permanent cures will result. We do not yet know, however, how soon after the operation to begin the treatment, how often to apply it, how long it should be continued, or what dosage to apply. We have assumed that it will do no harm. Recurrences take place in spite of this treatment, and, according to the writer's experience with irradiation of Hodgkin's disease, nodes which appear in areas that have been prophylactically irradiated do not respond as promptly as those occurring in areas that have not been previously treated. In Hodgkin's disease, also, after irradiation over long periods, injurious effects have been demonstrated at the autopsy table, on normal structures. In a case of mammary cancer, one year after operation, in which a few supraclavicular nodes had been the only evidence of the disease for several months, one application of *x*-rays to the chest wall and neck was followed in ten days by a rapidly fatal recurrence in the chest wall and pleura. While such observations do not condemn the procedure, the necessity is suggested for closer study of the effects of these agents upon normal tissues.

The preoperative treatment of mammary cancer is much less popular, but it appears to the writer to rest upon a more scientific basis than the postoperative application. From our

own observations we must believe that the injurious effects of the operation are thereby minimized. Numerous objections, however, to this procedure are offered by the surgeon, a few of which deserve our discussion. The objection that the healing of the wound is delayed is based apparently upon a few scattered observations. On the contrary, a prominent surgeon recently stated that he observed that after irradiation wounds healed better and left a better scar. A greater liability to wound infection appears to have some basis of fact. The writer has made several observations of a peculiar erysipeloid skin infection, occurring several weeks after treatment in the presence of an open wound, which suggests a relationship to the previous irradiation. The objection that the operation is made more difficult is the one most frequently offered, but, in the case of the breast, except for a slightly increased tendency to hemorrhage, if performed too soon, it is difficult to conceive that such an objection is valid. It is most often observed in connection with the performance of a hysterectomy for uterine cancer. It is usually based in this field upon an erroneous conception of the extent of the lesion before treatment. If there has been little or no extrauterine tumor tissue, there will be no hard tissue to cut through. If, however, as a result of the irradiation, a considerable amount of extrauterine tumor tissue has been converted into a fibrotic scar, the operation will naturally be difficult. A correct conception, however, of the original lesion would have shown that the operation was contraindicated. The general adoption of preoperative treatment in mammary cancer will soon show, I believe, that the field of applicability of the radical operation should be much restricted. It already seems to the writer that the presence of hard, fixed nodes in the apex of the axilla makes the cases as unsuitable for a radical operation as does the presence of supraclavicular nodes. It is a question how long it will be before the *radical* operation in mammary cancer will be entirely discarded.

The use of the *x*-ray and radium in the treatment of primary bone sarcoma is in the experimental stage, but a few facts have been definitely established, and our results suggest that, with greater accuracy of diagnosis, with an

improved technique, and with more frequent resort to the use of these agents prior to operative procedures, more substantial progress will be made. First, our work has confirmed the experimental results of the physical laboratory which show that the bone structures offer but little more resistance to the penetration of the rays of these agents than the soft tissues. The most substantial evidence of this is seen, in addition to the clinical improvement, in new bone production as demonstrated in the roentgenograms. As in the soft tissues, we have found that the effects depend upon the nature, size, extent and condition of the tumor. Infection and necrosis from overdosage are greater obstacles to success in bone tumors than in tumors of the soft parts. Bone tumors that responded well at first did badly after they had become infected. The type of the tumor is the most important factor.

In the malignant osteogenic tumors, which were most often of the periosteal type, our clinical results were practically negligible, except in one or two instances. In numerous cases, however, the evidence in the roentgenograms of new bone production, although often slight and temporary, showed that effects had been produced; and it leads us to hope that, by irradiating such tumors prior to amputation, the final results will prove to be better than they were when the operation was the only resource.

In the giant-cell tumors, or relatively benign giant-cell sarcoma, varying in type from those which closely resemble the osteitis fibrosa or bone cyst, to those in which their local extension and recurrence show considerably malignant qualities, our progress has been both encouraging and disappointing. Radium has been applied to the wound after curettage to prevent recurrence, and in numerous instances, the local recurrences after the operation, either by surface irradiation or by implantation into the tumor, have completely disappeared. Necrosis and infection, however, have often made the progress of repair slow, and, in a few cases, failure of the wound to heal, although the growth had been stopped, made amputation finally necessary. The results of the use of *x*-rays or the gamma rays of radium in tumors of this type, which were inoperable on account of their location, lead us to think that, with their earlier recognition by means

of the clinical history and *x*-rays, this form of therapy may ultimately prove to be an efficient substitute for incision and curettage.

In the progress of this work a tumor presenting clinically many of the features of a malignant periosteal sarcoma responded primarily to irradiation by the gamma rays of radium as promptly as lymphosarcoma. A similar response occurred in several other cases of bone tumor, all of which showed the same histological features which Ewing has described as endothelial myeloma. Although they differ from the characteristic features of each of these tumors, histologically and clinically they resemble both. From the *x*-ray standpoint they resemble giant-cell sarcoma and myeloma, but differ from each. In the long bones they begin in the shaft. Clinically, they occur in youth, are often multiple when first observed, and in general, present the picture of a malignant tumor. They are usually described as round-cell sarcoma of the bone. If, like myeloma, they have a multiple focus of origin, we may expect nothing more than a palliative result, which we obtain by the use of irradiation in that disease.

In conclusion, in addition to supplanting the operation as the method of choice in a number of fields of malignant neoplasm, the use of irradiation has so limited the field of applicability of the *radical* operation in numerous others that it is becoming a questionable procedure. In uterine cancer, it is entirely eliminated, and in mammary cancer, it is a question of accurate diagnosis.

The use of irradiation, therefore, has made necessary greater refinement in diagnosis than heretofore.

To this end, the patient's interests are best conserved by obtaining the conjoined knowledge of the surgeon and the radiologist. In fact, cancer therapy has become an institutional problem requiring, for the administration of physical agents, more clinical experience and knowledge of surgical pathology than does operation.

XIX

AN ANALYSIS OF RADIATION THERAPY IN CANCER[1]

THE MÜTTER LECTURE

JAMES EWING, M.D.

Only two definite epochs appear in the history of cancer therapy. One began with the Ancients and continued, practically unchanged in its conception, until about the beginning of the twentieth century. Its principle consisted in the complete removal of all cancer tissue, and for this purpose reliance has been mainly on the knife. From time to time the cautery, in one form or another, has contested the sway of the knife, but in spite of certain apparent advantages, it is probably not more popular today than it was in some previous centuries. A more consistent rival of the knife has been, from the earliest times, the caustic chemical, which today enjoys rather cool approval, but nevertheless, maintains itself in isolated circles as a worthy agent. All these methods aimed to accomplish the one object which alone was demanded according to prevailing theories of the nature of cancer, the direct removal from the body of the offending cancer cell.

Probably no other medical problem has through the ages received such searching attention or such skilful elaboration. As for the results, and the capacity of this therapeutic method to cope with cancer, few will deny that the verdict is "unsatisfactory." The mortality from cancer, as judged from statistics, has been but slightly influenced, while from the narrower viewpoint, that of the cancer patient, the same verdict must be returned. Nor does it seem likely that any improvements in surgical technique, or any fruits of the misconceived search for a supposed cause of cancer, will

[1] Read November 1, 1922. Reprinted from *Tr. Coll. Phys. Phila.*, 1922.

alter this conclusion; while the campaign for the early recognition of cancer offers hope in only a limited field. Established cancer will long remain the chief form of the disease.

At about the beginning of this century a new era slowly began in the treatment of cancer. In the course of a decade it was discovered that *x*-rays and radium exert a somewhat selective effect on proliferating tissue cells, and especially on tumor cells. In the course of another decade the methods of treating cancer by these physical agents have experienced a very extensive development, in connection with which an entirely new branch of scientific research and practical therapeutics has grown up. Are the bases of this new science secure?

The final answer to this question will probably be found to depend on the validity of the theory of the selective action of the gamma rays, for if it transpires that radium and *x*-rays are merely new and handy destructive agents or caustics, then the startling regressions and apparent cures of many cancers which inflame the enthusiasm of radiotherapeutists will be succeeded by an increasing proportion of late recurrences, the difficulties, dangers and sequelæ of radiotherapy will claim increasing attention, and radiotherapy will subside into a subordinate place in the treatment of cancer.

It also appears highly probable that unless radiotherapy conserves the natural resistance of the body against cancer, and fortifies its mechanism, even unless it increases the natural resistance and works *secundum Naturam*, in accordance with the physiological significance of the cancer process, it is destined to enjoy only a temporary popularity and will sooner or later take its place with the other empirical methods, such as surgical extirpation.

Do radium and *x*-rays exert a selective action on tumor cells? Bearing on this matter, there is first considerable clinical evidence. When a proper dose of filtered radiation is applied over a basal-cell carcinoma in the skin, this lesion has in many instances slowly disappeared, leaving little or no scar and not recurring after many years. Simliar effects have repeatedly been observed after similar treatment of many examples of the entire group of basal-cell carcinomas,

so that this group early became recognized as peculiarly susceptible to radiation. Similarly, lymphoid tumors, without apparently any exceptions, melt rapidly under adequate radiation, although secondary changes such as fibrosis may render such growths refractory. This rule also applies to a considerable variety of tumors related to the lymphoid group, such as endothelioma of lymph-nodes, endothelioma of bone and myeloma. In general, tumors derived from

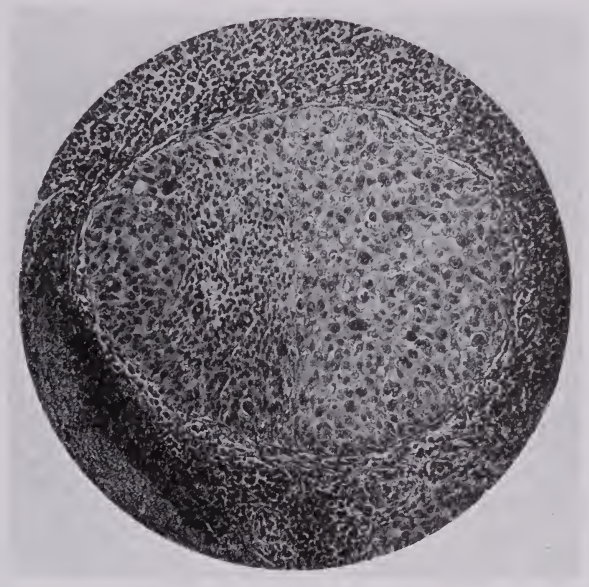


FIG. 41. Plasma-cell reaction about island of infiltrating carcinoma of bladder produced by local radiation in the bladder.

embryonal cells and retaining embryonal characters, even when growing rapidly, are, as a rule, particularly susceptible to radiation, and in this group some of the most remarkable and paradoxical of the radium cures have been recorded. Finally, it was early observed that very cellular rapidly growing tumors of any type, even when derived from adult cells, are often very susceptible to radiation, although the rapid extension of such tumors rendered the prognosis poor.

On the other hand, malignant tumors derived from adult cells and reproducing adult cells, such as squamous carcinoma,

neurosarcoma, osteosarcoma, many adenomas and other benign tumors, prove very resistant or quite refractory to radiation.

From all these clinical observations, which were quite new in medical experience, the conclusion was naturally drawn that radiation has a selective effect on some, but not on all, tumors. From them was formulated the first law of radiation therapy, commonly known as the law of Bergonié and Tri-

FIG. 42. Diffuse lymphocytic and plasma-cell reaction in endometrium following caustic effect of local radiation, in cases of cervical carcinoma.

bondeau, which may now be broadly stated as follows: Tumors composed of rapidly multiplying cells, especially those of embryonal type, and particularly those of the lymphoid group, are highly susceptible to radiation, and in such ratio as the above characters are developed.

Although there are many factors which enter into susceptibility to radiation, clinical experience has now extended sufficiently to permit one to classify tumors according to their radiosensibility.

Relative radiosensibility of tumors:

1. Lymphoma; lymphocytoma, lymphosarcoma, myeloma.
2. Embryonal tumors; carcinoma of the testis and ovary, basal-cell carcinoma.
3. Cellular anaplastic adult tumors; "round-cell" carcinoma, diffuse carcinoma.
4. Desmoplastic tumors; carcinoma simplex, fibrocarcinoma, squamous carcinoma.
5. Adenocarcinoma; adenoma of the uterus, intestine, breast, etc.
6. Fibroblastic sarcoma; osteosarcoma, neurosarcoma.

The clinical observations on the high susceptibility of certain tumors did not, however, prove the selective action of radiation. This is a problem for more refined methods of study which have not yet provided a final solution.

The microscopical changes that follow the application of radium to a susceptible tumor strongly support the theory of a selective action. These changes have been described by so many observers, and are so well known, that it is unnecessary to review them in detail. They consist of swelling, hyperchromatism, vacuolar degeneration and solution or fragmentation of nuclei, hydropic swelling, vacuolation and solution of the cytoplasm. Mitotic nuclei are particularly vulnerable, the chromosomes splitting, the spindle threads disintegrating and the whole cell undergoing relatively speedy solution. The surrounding stroma exhibits hyperemia, slight serous exudation, outwandering of leucocytes and growth of new capillaries which in many instances probably plays a prominent part in the removal of tumor cells. The stroma cells may exhibit to a slight degree the same changes as the tumor cells, but it seems clear that the action on the stroma cells, in this, the ideal form of radium reaction, is mainly stimulative and not destructive. Ideal radium therapy seems to require a nice adjustment of relations between destructive effect on tumor cells and stimulation of stroma cells. Opinions differ as to whether the action is mainly on the nucleus or on the cytoplasm, but it undoubtedly affects both, and probably in variable degree. The whole process seems to represent a peculiar form of autolytic degeneration. By what physical and chemical processes the changes are brought about we do not know. The chemistry of radiated

tumors has not been determined. There is reason to believe that cell constituents are ionized and intracellular ferments activated, so that reactions readily occur which otherwise would not occur at all. It is obvious that this theory, if correct, definitely supports the view that the reaction to radiation is specific.

Whatever its nature, I find no reason for altering the conclusion expressed in 1916 that the series of changes occur-

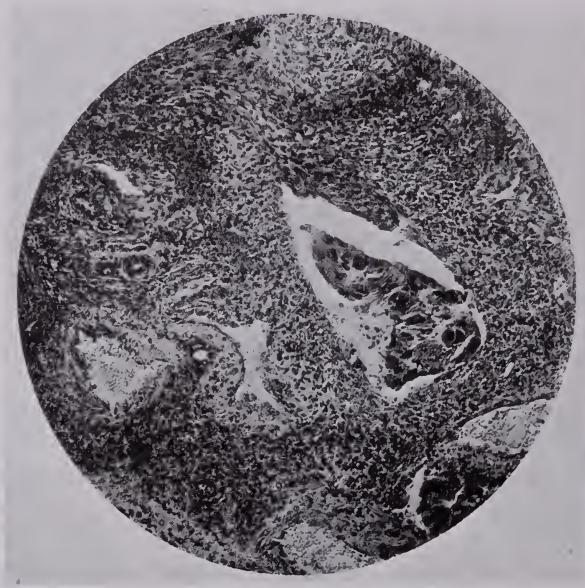


FIG. 43. Lymphocytic and plasma-cell reaction in squamous carcinoma of cervix invading parametrium, from local radiation through vagina.

ring under these and in more severe forms of radium reaction, taken as a whole, are not duplicated under any other conditions and indicate a specific and selective action of radium upon tumor cells. Very similar changes are produced by *x*-rays, but I have drawn the impression that *x*-rays, as usually employed, are less selective in their effects and tend to produce more destruction of stroma and blood-vessels. If the above observations are correctly interpreted then radium therapy fulfils one of the requirements of a rational therapy, acting *secundum Naturam*. Under certain conditions

here designated as ideal radium therapy, it exerts a selective action on certain tumor cells and causes their disappearance by autolysis.

But it soon became apparent that most tumors cannot be made to disappear by moderate external radiation which fails to destroy the overlying skin or mucous membrane and the surrounding stroma. Squamous carcinoma, one of the main goals of radium therapy, has notoriously resisted

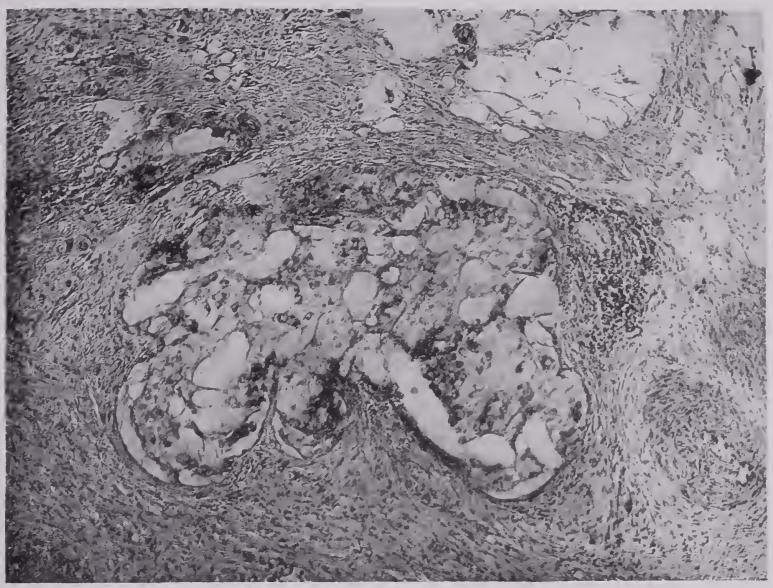


FIG. 44. Adenocarcinoma of rectum. Vacuolar degeneration of tumor cells five weeks after insertion of bare emanation tubes in the vicinity.

external radiation. It may recede, but it generally recurs after repeated external raying; and it was not until an essentially different and much more intense action was employed that any definite success was achieved in the treatment of squamous cancer. This method consists in employing radium as a caustic.

Apparently it was Stevenson, of Dublin, who about 1915 first inserted coarse needles containing radium into the substance of squamous carcinomas of the mouth and of the tonsil and left them there long enough to cause sloughing of

the tumor. He thus succeeded in curing some of these cases. About the same time Weil and Janeway employed the same method at the Memorial Hospital. Duane improved the method by using small amounts of emanation in capillary glass needles and leaving them in the persisting edges of rodent ulcer. To Janeway belongs the credit of perfecting the method and employing it on a large scale with squamous carcinomas of tongue, tonsil and many other tumors.

FIG. 45. Extensive hornification of squamous carcinoma in ischiorectal fossa in case of anal carcinoma, by local implantation of radium emanation needles.

Lingual, buccal and tonsillar cancer, uncontrollable by other methods, yielded in a high proportion of cases to this procedure. Finally, Quick pursued the plan still further by inserting the needles into infected lymph-nodes, where they remained permanently, becoming surrounded by dead tumor tissue and thickened capsules. This method has greatly extended the scope of successful radium therapy and is applicable to a wide variety of resistant tumors. The danger of disseminating viable tumor cells by the insertion of the

needles is reduced by a preliminary surface radiation. The pain is considerable, but less than that which follows strong surface radiation of the mucous membranes.

The caustic action of radium may also be secured by the interstitial injection of radioactive deposit in salt solution. The solution diffuses over a rather wide territory, but is limited by the capsules of glands and tumors. It exerts a slow necrotizing action, followed by considerable cellular

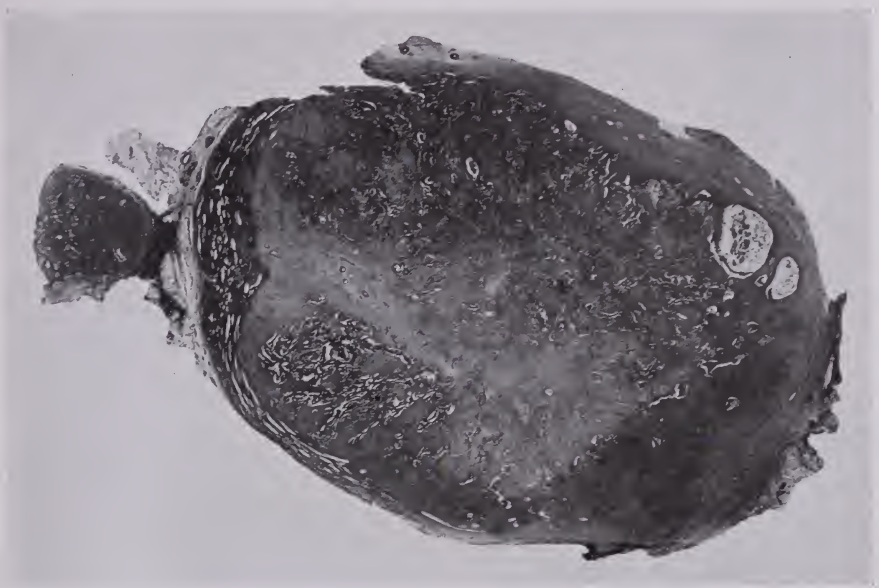


FIG. 46. Cervical lymph-node invaded by squamous carcinoma of tongue. Treated with bare emanation tubes three weeks before removal. Extensive destruction of tumor cells, diffuse fibrosis, thickening of capsule. Small groups of tumor cells are still visible.

exudation, but without constitutional disturbance. It permits the full action of all the rays of radium, alpha, beta and gamma, and is thus much more powerful than any form of filtered radium. It is applicable especially to encapsulated tumors or encapsulated organs, particularly the lymph-nodes. It has been employed as an intravenous injection in leucemia and lymphosarcoma. The method has many

peculiar advantages and deserves more attention than it has yet received.

Regaud, of Paris, hesitates to adopt the caustic method, because, as he says, it is not true radium therapy; but he acknowledges failure to cure lingual cancer by other means. Each radium needle containing 1 mc. of emanation produces a zone of necrosis about 0.5 cm. wide, but a sterilizing action extends at least 1 cm. wide. Each tube of 1 mc. of emanation yields the equivalent of 133 mc. hrs. of radiation in

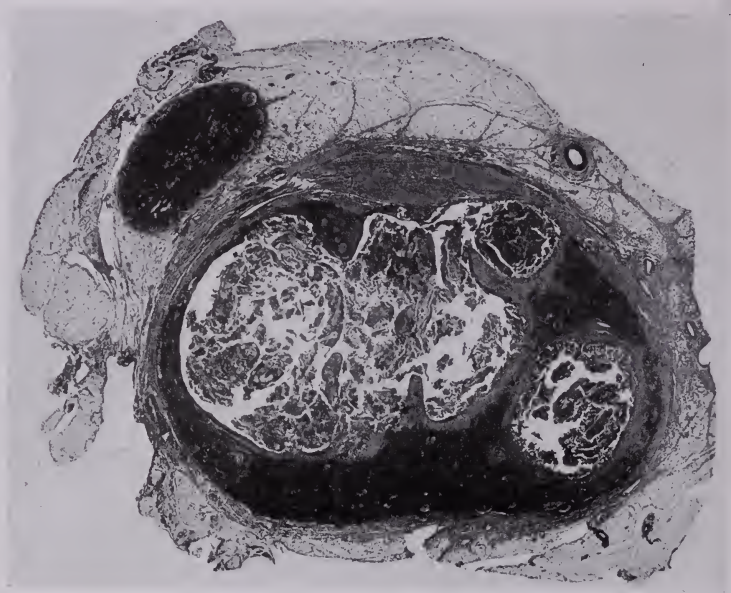


FIG. 47. Squamous carcinoma in lymph-node. Destruction of tumor tissue, fibrosis of capsule and preservation of uninvolved lymphoid tissue, one month after insertion of bare emanation tubes.

the course of its life. After fifteen days it reaches 1 per cent of its original strength, from which point further decay is slow. When fifteen to twenty tubes are employed the total amount of gamma radiation is considerable. It is probably this gamma radiation, sterilizing a wide territory, which is responsible for the clinical success and which renders radium the best caustic ever devised for cancer. Regaud's objection is thus partially met.

It is highly important to recognize that radiation therapy is no longer confined to the original simple autolytic process which controls many embryonal tumors, that it confesses failure to deal with many more resistant tumors by this method and resorts to the caustic action, markedly exhibited by the alpha and beta rays, in dealing with many forms of cancer.

The structural changes following the caustic action of radium support the view that this reaction is specific. This

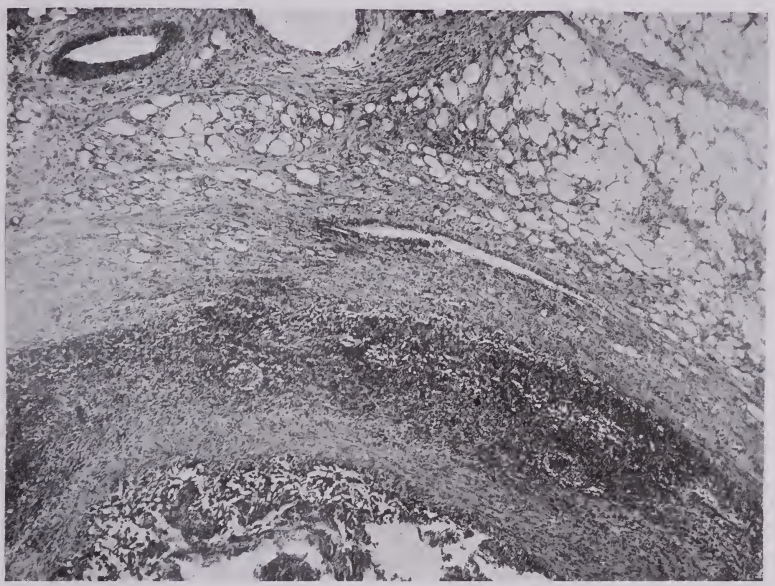


FIG. 48. Squamous carcinoma in lymph-node. Destruction of tumor tissue and fibrosis of capsule of node, one month after insertion of bare emanation tubes.

method has long been used in the treatment of cervical uterine carcinoma by placing radium tubes in the uterine canal until ulceration and necrosis follow. Here the cellular reaction is striking and peculiar. The tumor cells undergo extreme changes of the type previously described. They eventually undergo solution or form giant cells and syncytial masses in which polynuclear leucocytes penetrate and complete the absorption. Often structures strongly resembling

miliary tubercles are produced. There is a very notable exudation of plasma cells which completely replace the eroded mucosa, while lymphocytes, large and small, are often present in the exudate. The small blood-vessels immediately beneath the eroded mucosa and about the foci of degenerating tumor cells proliferate and seem to excavate actively the nests of degenerating cells. Deeper blood-vessels undergo obliterating arteritis, which shuts down the blood

Fig. 49. Hornification and desquamation of cells in squamous carcinoma in lymph-node. External radiation.

supply and eventually produces general shrinkage of the tissues. This type of reaction I have not seen duplicated under any other conditions.

In dealing with basal-cell carcinoma of the skin and with squamous carcinoma of accessible mucous membrane, the procedures above described have been found to yield such uniform results that the treatment of these diseases may be said to have passed beyond the experimental stage and the methods to have become practically standardized. But when one comes to deal with the great number of tumors

which lie deeply beneath the skin or in the thorax or in the abdomen, one enters a very complex field in which all the resources of physicists and radiologists have failed to secure satisfactory results, and in which opinion on essential matters is in a state of considerable confusion.

Out of this mass of data I think one can extricate and emphasize one principle of radiation therapy which is of the first importance. It has long been observed that when one

FIG. 50. Mammary carcinoma treated with bare emanation tubes. Destruction of tumor tissue, lymphocytic invasion, fibrosis and calcification. The small cells are lymphocytes.

radiated certain deep-lying tumors of the more resistant class, such as adenocarcinoma of the corpus uteri or osteosarcoma of bone, the tumors failed to disappear, but their growth was inhibited and the tumors remained in a state of suspended growth with somewhat altered structure of a less malignant type. It has even been claimed that an adenocarcinoma might be converted into a harmless adenoma. Under such treatment I have observed an osteosarcoma become converted into a solid, quiescent, highly osseous tumor.

These observations indicate that radiation is capable of restraining the growth of tumor cells without causing either autolysis or necrosis, and of transforming functionless lawless cell growths into more organized and functioning tissues. This action is exerted also on proliferating connective tissue and on a wide variety of simple inflammatory and functional hyperplasias, and forms the basis of radiotherapy in many diseases outside the realm of tumors. If these deduc-

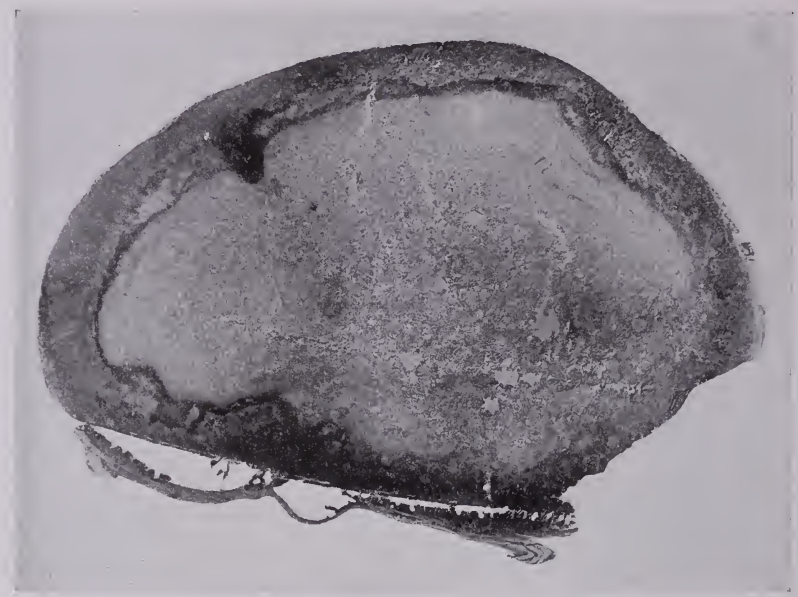


FIG. 51. Rat sarcoma treated by injection of radium deposit, showing diffuse simple necrosis. Removed after ten days. (After Bagg.)

tions are correct, then this property of radiation is an extremely important addition to general therapeutics. For the first time in the history of medicine we are in possession of an agent which will control the growth of connective tissue. This tissue is the main element in the lesion which underlies many chronic and practically irremediable diseases, so that the search for such an agent has been the faint hope of pathologists for many decades. Aside from the practical question of its successful application, this property of radiation is of very great scientific interest. For this property we

may safely conclude that its action is both specific and selective. Normal tissues and organs are distinctly less sensitive than neoplastic and hyperplastic. Even normal lymph-nodes resist radiation when inflammatory hyperplasias yield readily. We may also claim that its action is *secundum Naturam*, in that when properly employed it inhibits that reaction in excess which Weigert emphasized as the significant physiological element in productive inflammation and which exists also in many neoplasms.

FIG 52. Cavity from liquefaction necrosis and area of simple necrosis produced by radium emanation needle in muscle tissue of rabbit. (After Bagg.)

We have thus reviewed three main principles of radiation therapy which appear to be fundamentally different, and each of which is selective, specific and tends to support natural processes of defense. These are:

1. Autolytic degeneration, observed mainly in the group of embryonal tumors.

2. Caustic destruction, employed in the treatment of resistant adult squamous carcinoma by bare radium emana-

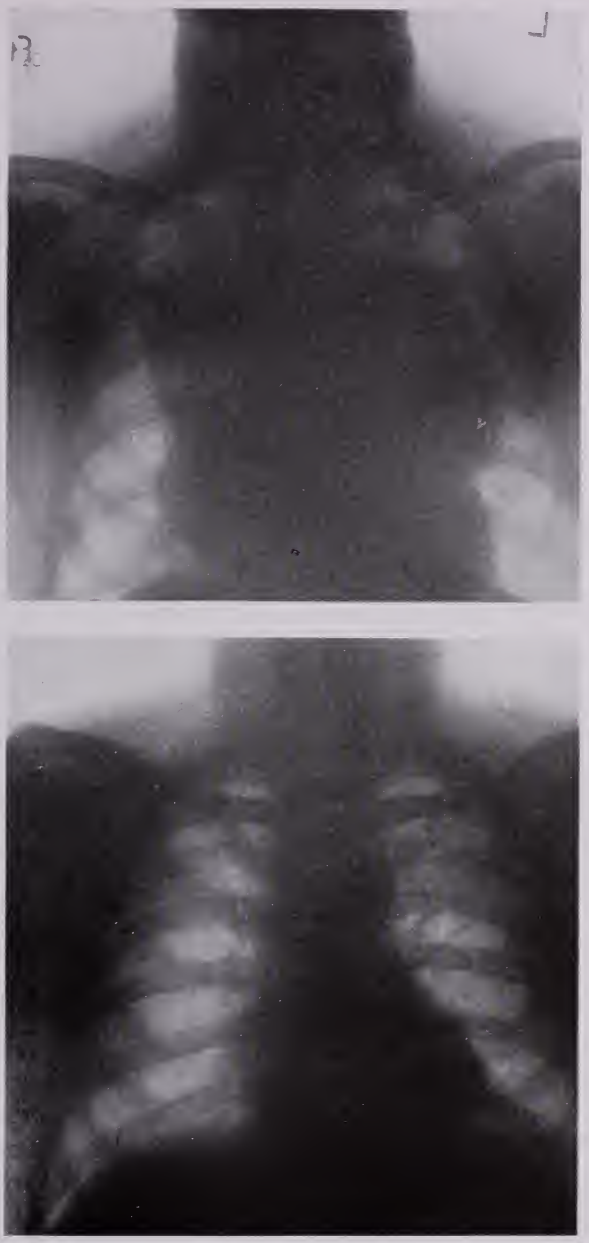
tion tubes, active deposit of radium and heavy doses of hard gamma and *x*-rays.

3. Growth restraint, illustrated in the slow recession of resistant tumors under deep radiation and in the treatment of chronic inflammatory hyperplasias.

In further support of the view that radiation therapy tends to employ and support Nature's methods of healing, we may consider at this point whether the regression of a tumor

FIG. 53. Reaction about emanation needle in brain tissue of dog. From left to right: normal brain tissue; cellular area of lymphocytes and new vessels; zone of leucocytes; zone of necrotic tissue; cavity of the needle.

tissue under radiation may not increase the local and general immunity against cancer. We know very little about natural immunity or resistance to cancer, but clinical experience and experimental data show that there is such a physiological property in the organism. The most direct experimental evidence was obtained first by Gaylord and Clowes, who observed that animals in which spontaneous absorption of tumors had occurred became much more refractory to implantation. I recall that dogs which had recovered from the



b

FIG. 54. Mediastinal tumor, probably thymic, *a*, eighteen months before and *b*, eighteen months after *x*-radiation. Illustrating slow autolytic degeneration.

infective lymphosarcoma after injection of normal blood became quite refractory to this quite viable tumor. When, therefore, a bulky tumor in a human subject is caused to

FIG. 55. Periosteal osteogenic sarcoma before and after *x*-radiation. Illustrating growth restraints.

regress under radiation and its autolytic products are absorbed, we seem to have an exact parallel to the experimental immunization of animals. Whether the resulting immunization, if it occurs at all, is sufficient to prove of practical importance, can only be determined by long clinical

experience; but radiologists are certainly justified in looking carefully and critically for such results and in assuming their probable occurrence. One may regard the apparent postponement of metastases in partially regressing malignant tumors as evidence of increased immunity, just as one concludes that resistance is diminished when, after the extirpation of a primary tumor, hidden metastases often spring up rapidly and exhibit increased growth capacity. Apparently the body can produce only so much tumor tissue in a given time, and when a primary tumor exhausts this capacity the progress of secondary growths must be limited. All these considerations, which at present lack definite form, open up new points of view regarding the physiological significance of the cancer process and must have an influence on therapeutic conceptions of the future.

DOES RADIATION EVER STIMULATE TUMOR GROWTH?

Any adequate answer to this question must recognize the complexity of the problem involved. The question is raised by clinical radiologists who have observed very rapid recurrence and widespread extension of unsuccessfully radiated tumors and who naturally suggest that improper radiation may actually stimulate the growth of tumor cells. The most striking cases are those in which long-continued radiation fails to destroy the tumor cells and produces much scar tissue, in which tumor cells persist, and from which they eventually extend, often with considerable activity, into surrounding tissues. Occasionally this is followed by unusually rapid generalization of the disease. The explanation of these cases is a complex pathological problem.

It is said that prolonged radiation may transform the relative susceptibility of tumor cells and stroma, so that the tumor cells become more resistant than the stroma. I have seen well-stained and apparently viable cells of squamous carcinoma lying long persistent in heavily radiated hyaline acellular scar tissue. I think the better explanation is that the tumor cells actually do become resistant, but mainly because they are protected from the natural defense reactions which cannot take place in acellular, nonvascular scar tissue. Obliterating arteritis which follows prolonged radiation

paralyzes these defense reactions over a wide territory in which tumor cells may later grow without restraint. Chronic infections often become established in such tissues and facilitate the spread of the tumor process. Finally, prolonged radiation undoubtedly may injure the whole organism, especially the blood-forming functions, so that to the tumor cachexia is added the damage of prolonged radiation, producing those rapid terminal extensions of the disease which many observers have regarded as accelerations of growth from the stimulating effects of radiation. I have performed autopsies on several such cases and have been much impressed by them, but I am not convinced that equally rapid terminal extensions do not occur without previous radiation. As a very uniform rule autopsies on radiated cases reveal much less tumor tissue and much more fibrosis than we were accustomed to see before the advent of radium. In such enfeebled subjects tumor cells may grow without restraint. Radiologists are agreed that cachectic subjects seldom do well under any form of radiation.

There is much experimental evidence to show that small doses of rays accelerate growth by stimulating mitosis and intracellular metabolism. Vegetable seeds have germinated more rapidly and plants have doubled in size under *x*-ray influence. In animals the results are much less convincing and many complicating factors enter into the experiments, so that one may accept with considerable hesitation the law formulated by Arndt that small doses stimulate while large doses kill the cells.

From the extensive literature on this subject I draw a somewhat uncertain impression. Thus, Hoffman exposed frog larvæ to 20 to 40 per cent of the erythema dose of *x*-rays and found that the majority of individuals showed moderate definite increase in size and increased metabolism. This condition continued for two weeks, and then diminished, and after three to eight weeks the animals could not be distinguished from controls. Yet in two experiments only diminished growth and injury were observed. When the animals were placed in 10 per cent sugar solution even 10 per cent of the erythema dose always caused injury. It thus appeared that stimulation effects depended on the chance of

applying just the right dose to animals in just the right condition. Failla and Suguira saw definite acceleration of growth in young mice exposed to small doses of radium.

While O. Hertwig saw acceleration of the mitotic process in eggs of Ascaris megalocephala, the doses employed were extremely minute. The numerous studies on the effects of radiation of embryos reviewed by this author in "Lazarus's Handbuch d. Radiumbiologie u. Therapie," all indicate that embryonal cells always receive injury and inhibition even with very small doses of radium rays. Murphy seems to have succeeded in increasing the number of circulating lymphocytes by applying small doses of *x*-rays over the spleen and the marrow of guinea-pigs; but it seems probable that this increase, in so far as it surpasses increased mobilization of preexisting cells, is the result of regeneration after injury of these cells and tissues.

The main practical conclusion I wish to draw from all these data is that the danger of stimulating the growth of tumors by the present methods of radiotherapy is extremely remote, while the idea that inadequate radiotherapy can endow the cells with increased vitality is quite unreasonable.

DEEP RADIOTHERAPY

The most difficult problems of radiation therapy have arisen in the effort to deal with deep-lying tumors, either primary or secondary. During the past few years and up to the present time this has been the great field of investigation, debate and experiment, as it will probably remain for many years to come. At present the physicist dominates the situation. Observing that superficial or accessible tumors may generally be made to disappear by adequate and generally severe radiation, the physicist has been called upon to devise means of delivering the same dosage at various depths in the body without injuring the skin. According to Kepler's law, the amount of energy received at any point varies inversely as the square of the distance, so that it became necessary to increase the source of energy, the distance, the filtration and the time of exposure. The radium pack, containing two or more grams of radium, and the modern high-voltage *x*-ray machine are the two methods

employed to deliver the necessary energy to the deeper tissues.

From the physical point of view the results have been highly successful. In all large clinics data are available by which it is possible to compute accurately just what elements must be provided in the dosage to deliver at any point in the body the required energy. Since, according to physical conceptions, the physiological effect is exactly in proportion to the atomic weight of tissue elements, it is possible under most circumstances to compute the effective dosage. Rather implicit reliance has been placed, especially in Germany, on the theory that if the so-called killing dose has been delivered the tumor must disappear. Thus we have the expressions, "carcinoma dose" and "sarcoma dose," the former considerably above and the latter generally below the erythema dose. Seitz and Wintz originated and still adhere to the idea that there is a standard carcinoma dose that they place at 90 to 110 per cent of the erythema dose, which is the least amount that can properly be employed in dealing with deep carcinomas. The sarcoma dose ranges from 60 to 80 per cent of a carcinoma dose. Although this conception has been vigorously attacked by many German roentgenologists (Werner, Jungling, Perthes), it has had considerable influence if not a controlling effect on the deep therapy of the present time.

Several expedients are employed to intensify and increase the depth dose without injuring the skin and other normal structures. Two and even three sources of rays may be employed simultaneously. Numerous skin portals are arranged through which at successive times the rays may be centered upon the deep tumor. The influence of scattered rays, those developing within the tissue, have been found to be highly important, and various expedients are employed to increase these rays.

Concentration of Scattered Rays. When a beam of *x*-rays passes through tissue it loses by absorption at the surface and at all levels in the tissue, in addition to the diminution dependent on the inverse square law. It also loses by the scattering of the rays as they impinge upon tissue molecules. On the other hand, if a sufficiently large volume of tissue is

irradiated, the scattered and secondary radiations will effectively increase the depth dose. These losses are partly compensated by the development of secondary rays produced by the impact upon tissue molecules. Both the scattered and the secondary rays increase with the hardness of the original rays. They also necessarily increase with the breadth of the original beam, and correspondingly if two tubes, both yielding broad beams, are employed.

Chaoul has endeavored to increase the effect of scattered rays by enclosing the body or limb in paraffin in a square 20 × 20 cm., by which the rays from a wide territory are "collected," as it were, and turned into the tissues from all sides. By this means also the radiation becomes more nearly uniform at distances from the center of the beam. By using such apparatus, with 210,000 volts at 50 cm. distance, 1 mm. copper filter, two portals, he secures at 20 cm. depth 90 to 93 per cent of the skin dose. The therapeutic results of this method are not yet known, but from the physical side it is obviously of much promise.

All these details of the modern deep therapy have been ingeniously conceived and skilfully employed with the idea of delivering the killing dose to the deep tumor, and upon the theory that the heavier the dose the better the result must be. It is too early to formulate definite conclusions regarding the clinical success of deep radiation therapy, although certain principles seem to be defining themselves in this field; but it is certainly advisable that the principles on which deep radiation is based should be carefully scrutinized.

From the study of much material, from operation and autopsy, in cases treated by deep radiation, I have become convinced that the clinical results are not usually due to the direct killing effect of radiation, but are generally brought about indirectly and mainly by interference with the circulation—capillary, venous, arterial and lymphatic. This conclusion is in accordance with the rule of pathology that acute necrosis of tissue cells generally means interference with blood supply. In the examination of many bulky cellular tumors of the thorax and the abdomen, which regressed rapidly under radiation, one finds broad areas of simple or liquefaction necrosis, mainly in the center of the tumor,

which can only be explained as the result of infarction, while small cell groups on the periphery of the tumor appear well preserved and little affected. If the surviving cells are viable the tumor recurs, but in certain cases these cells are not viable—they slowly degenerate and a clinical cure results. In any case the main part of the destruction has been caused by occlusion of blood-vessels. In the case of most deep-lying infiltrating and desmoplastic carcinomas there is less opportunity for infarction and the tumors do not regress rapidly. Such tumors exhibit isolated foci of necrotic cells, marked hydropic degeneration, interstitial hemorrhages, granular and mucinous degeneration of collagen fibrils, but usually some areas in which the cells appear well nourished and viable. After several weeks, sclerosis of injured blood-vessels appears, which shuts off the circulation. The tumor tissues then undergo progressive fibrosis, but usually groups of tumor cells persist in the scar tissue and later give rise to recurrences. From many observations of this type I have drawn the conclusion that it is very difficult to destroy the average deep-lying carcinoma and that the so-called sterilizing or killing dose is considerably higher than it is generally placed.

Not all deep tumors, however, escape with remnants of persisting cells. Some yield completely to deep therapy, and these are almost invariably of embryonal type, as carcinoma of the testis, or of lymphoid character, as lymphosarcoma or myeloma. I have also seen complete regression and fibrosis of soft fascial myxosarcoma in the pelvis. With certain embryonal tumors of the kidney in infants (Wilms' tumor), one-quarter of the erythema dose has been found to cause very rapid regression of the tumor and serious collapse of the infant patients.

Nevertheless, the usual failure to eradicate completely malignant tumors by deep therapy leads one to conclude that this method of attack will gradually be replaced by the exposure of the tumor and more direct application of the agent, especially the insertion of radium needles in the tumor tissue. In this way it will be possible to injure the tumor while sparing the surrounding tissues.

The theory that it is best to deliver a killing dose of filtered radiation to deep tumors is not supported by clinical results.

These results, with the exception of certain very sensitive tumors, are distinctly disappointing. Moreover, they are accomplished very often with so much disturbance of the vitality of the patient, and with such frequent damage to intervening normal organs, that there appear to be distinct limitations to this method of treatment. Not infrequently, when the tumor has been successfully radiated from the physical standpoint, the patient dies from hemorrhage into or about the tumor, or from severe infection in the degenerating tumor tissue, or from absorption of secondary decomposition products of the tumor. The slower absorption of ordinary autolytic products is usually accomplished without any signs of intoxication, and there is no good reason to believe that intoxication results from limited areas of aseptic necrosis so long as the material remains free from infection and secondary decomposition.

On the other hand, when one proceeds in deep therapy on the theory that therapeutic results depend not only upon injury to tumor cells but also upon defense reaction of the body and the tissues, the immediate results seem to be almost equally striking, the end-result is often more satisfactory and the treatment is conducted with less damage and danger to the patient. By employing less than the killing dose and repeating the exposures at intervals, most of the embryonal and lymphoid tumors react as well as with very heavy dosage. With an *x*-ray voltage of 90,000 and with properly filtered radium packs at 6 to 10 cm., giving 9000 to to 20,000 mc. hrs., we have been observing for some years at the Memorial Hospital satisfactory regression of this class of tumors, many patients remaining free from demonstrable recurrence up to the present time. These results have been accomplished without notable disturbance to the patient or injury to the skin. The cases include abdominal metastatic carcinoma of the testis, embryonal tumors of the ovary, lymphosarcoma, Hodgkin's granuloma, leucemia, mixed tumors of the salivary glands, giant-cell tumors of bone, cellular osteogenic sarcoma and myeloma. The oldest of these cases, a teratoid tumor of the ovary, in a girl of eight years, is now of seven years' standing, and the patient is a healthy young woman, menstruating normally.

The process leading to these results has certainly not been the direct destruction of tumor cells. Many of the cases have required repeated exposures, and long periods often passed before the outcome was determined. It seems more probable that slow autolysis and growth restraint, aided by the natural defense reactions of the body, combined to bring about a gradual regression and eventual disappearance of the tumors. With the more adult and resisting tumors, such as recurrent mammary cancer, extensions of uterine cancer, corpus carcinoma, gastric and intestinal carcinoma and most osteogenic tumors and sarcomas, external radiation has been mainly palliative, growth restraint has been effected, the tumors have long remained quiescent and sometimes harmless, the life of the patient has been prolonged, but the tumor has not been eradicated. That better results will come from the higher *x*-ray voltages, 250,000 and more, with corresponding technical adjustments, or with radium packs at 15 cm., delivering 40,000 mc. hrs.' continuous exposure, seems not improbable. The present reports from these extremely intense treatments are in many respects highly encouraging, but the good results obtained may not be hastily attributed to the killing effects of the high dosages.

Finally, the uniform experience that no form of radiation yields any great success in debilitated or cachectic subjects emphasizes the principle that radiation therapy, rationally conducted, relies heavily upon the healthy reaction of the affected tissues and the whole organism. From these data the following general conclusions regarding deep therapy seem to be justified:

1. The physicist having provided instruments yielding high and controllable dosage, the use of the instruments is strictly a medical problem.

2. The successful treatment of deep tumors requires the careful adjustment of dosage to the individual case, with due regard to the age and condition of the patient, the type, structure and natural history of the tumor, and the relations and functions of the affected and surrounding organs. Every tumor is a study by itself. No uniform carcinoma or sarcoma dosage can ever be established. Results will not improve merely with increase of dosage.

3. Deep therapy cannot safely proceed on the theory of direct killing of cancer cells. Slow autolysis, growth restraint, focal necrosis from anemic infarction, reduction of blood supply, encapsulation and fibrosis are the most effective processes excited by deep radiation.

4. With the exception of embryonal, very cellular and lymphoid tumors the results of deep radiation are generally unsatisfactory, and palliation rather than cure is usually the safer goal.

5. On account of these limitations the progress in the treatment of deep tumors will probably turn more and more in the direction of exposing the tumor and applying the agent more directly.

ADJUVANTS TO DEEP RADIATION THERAPY

Recognizing the limitations of radium and *x*-rays in dealing with deep tumors, many workers have endeavored to fortify the radiation by several expedients.

Sensitization by Iodin. It has long been known that iodin administered by the mouth tends to be deposited in tumor tissue, partly uniting with glycogen and partly filtering out in degenerating tissues. Jess reports that after injection of iodin in considerable doses for several days, subsequently to disappearance of iodin from the urine, 71.6 per cent remains in the body. Since iodin yields characteristic secondary rays, administration of this agent may possibly intensify the effects of radiation. Although this expedient has been employed by several workers, there are no satisfactory reports as to its efficiency.

Iodides have long been employed in the treatment of malignant tumors, and rarely one sees remarkable regression of cellular tumors during its use.

Iodin stimulates the function of the thyroid gland, and since thyroid extract has had a long history in cancer therapy, not without results, it may act secondarily in this manner.

Schwartz suggests that the main dose of radiation be given at the height of the hyperemia produced by a preliminary dose, and he would further employ injections of tumor autolyzates at the same time.

A considerable variety of metals, simple and colloidal, and of organic extracts have been employed, by local and intravenous injection, to stimulate blood formation and render the tumor more susceptible. Kupferberg claims to have tried and abandoned them all, and regards as valuable only blood transfusion.

Wetterer treated a cachectic case of gastric carcinoma with deep therapy, and at the same time with blood transfusions from the patient's twenty-one-year-old daughter, and saw very striking improvement in the tumor and in all symptoms which had not been relieved by raying alone.

In 1910, I found de Keating-Hart in Paris, packing tinfoil into the recesses of a very extensive rodent ulcer, connecting it with another electrode on which the patient lay, and turning on the electric current until the patient complained of heat. He stated that it was impossible to cure such advanced cases with *x*-rays alone, but that they sometimes yielded completely when the temperature was raised. There are many limitations and several hazards connected with the artificial elevation of the temperature of tumors, especially from hemorrhage, but the influence of heat as an adjuvant to radiation has not received the attention it deserves.

All these studies, aimed primarily to intensify the effect of radiation, while they may not yet have yielded definite results, are of much theoretical interest. They probably indicate the direction in which progress is to be made in the future, and they seem to the writer more rational than the effort to increase steadily the dose of radiation.

THE INFLUENCE OF RADIATION THERAPY ON THE KNOWLEDGE AND CONCEPTION OF TUMORS

Experience with radiotherapy has forced workers in this field and surgeons and pathologists generally, to pay much closer attention to the natural history of specific neoplastic diseases. Indeed, many new facts and principles of tumor growth have been brought to light and emphasized which before were only vaguely appreciated. No one can safely engage in this work without considerable acquaintance with these matters.

The distinction between embryonal and adult tumors forms a very sharp line of cleavage in the results of radiation,

and must be carefully considered in establishing the correct dosage and estimating its effects. Not only rodent ulcer, but the entire extensive group of basal-cell carcinomas, including salivary gland tumors and cervical carcinomas, run true to form in respect to radiation. Many other tumors, at all ages, which have yielded promptly to radiation have taken their place among embryonal tumors, although previously their nature was not generally appreciated.

The distinction between embryonal and cellular anaplastic tumors is equally important, though much more difficult to detect; but until this is done many radiologists will continue to meet surprises and disappointments. Thus a very cellular anaplastic mammary cancer will resist most efforts at local destruction and will regularly kill by generalization, while an equally cellular embryonal tumor may melt down rapidly and neither recur nor generalize. On account of this embryonal character, most tumors in children do better than expected, so that aggressive therapy cautiously employed is generally advisable at such ages. On the other hand, nearly all the round-cell carcinomas of adults are anaplastic adult neoplasms with very unfavorable prognosis.

The desmoplastic properties of tumors, with the production of much stroma, without much regard to the character of the cells, render the tumors highly resistant. To bring such growths to a standstill without marked reduction in size, is all that can be generally hoped for, and for this purpose the caustic action of radium or *x*-rays is usually needed. Thus fibrocarcinoma may recede but seldom disappears under external radiation, and seems to require radium needles.

It has been necessary to give new emphasis to the differences between many fibrous tumors which are difficult to explain. Keloid and fibromyoma uteri respond to radiation to a degree which their structure did not suggest, while neurofibroma in all its phases proves extremely resistant. On the other hand, fascial sarcoma, which is difficult to separate clinically from neurosarcoma, is very sensitive to radiation on account of its richness in delicate capillaries, which are absent in neurosarcoma.

The variable response of different tumors to radiation constitutes an important department in radiotherapy which is of much value in diagnosis. The therapeutic test critically applied serves to distinguish sharply between many tumors which cannot be separated clinically, has greatly extended the means of diagnosis of tumors and reduced the indications for biopsies, laparotomies and frozen sections. Mainly by this means I have recently been able to call attention to the existence of a specific group of round-cell tumors of bone which had previously been submerged under the term "round-cell sarcoma," but which differ from cellular osteogenic sarcoma in being very susceptible to radiation.

The radiologist must not only be familiar with the structural and biological differences between the various classes of tumors, but he should be able to visualize the peculiarities in structure in different cases of the same tumor. Compare, for instance, two tumors of the testis which may be found of exactly the same size. One is a slowly growing, hard, adult teratoma composed of epidermoid cysts, cartilage and adenocarcinoma (Curling's hydatid disease). The other is a more rapid growth, firm but elastic, and consists of embryonal carcinoma with lymphoid stroma. The former will resist all attempts to reduce its size, but it will seldom recur if excised after radiation. The latter will disappear rapidly under radiation, greatly impressing the operator, but soon recurring in the abdominal lymph-nodes. Hodgkin's granuloma in its early stages is soft and cellular and will completely disappear under moderate radiation; but in late stages the lesion becomes firm and fibrous and under radiation the tissues are transformed into dense resistant cicatricial masses. Similar changes occurring naturally in the course of tumor growth have led to the unwarranted conclusion that the cells have acquired a new resistance to radiation.

Radiation of abdominal tumors should always be guided by a consideration of the structure of the tumor. One may safely deliver a heavy dosage to myomas of the uterus and to most lymphosarcomas, but I have seen three sudden deaths from hemorrhage into heavily radiated bulky abdominal metastases of testicular tumors which contained many large

blood sinuses. In attacking tumors of bone or cartilage the operator must proceed with the knowledge that exposed or ulcerating cartilage will never heal.

The importance of the general vitality of the patient is emphasized when the radiologist finds all his efforts fruitless in debilitated and cachectic subjects. Arteriosclerosis, syphilis, anemia and diabetes are among the general diseases that affect the vitality of patients, but they are seldom considered as factors influencing the results of radiation. Local arteriosclerosis is probably responsible for many excessive reactions, for delayed secondary sloughing of tissues, hemorrhages and the persistence of indolent ulcers.

Indeed, successful radiotherapy demands the employment of a broad, general, clinical knowledge upon which the operator must constantly draw in controlling the use of the powerful agents now at his disposal. All these considerations justify the statement that the developments of radiotherapy have opened up a new biology of tumors, stimulated many new lines of research and suggested new conceptions regarding the physiology of tumors.

Will the body withstand unlimited exposure to radiation? It has long been observed that patients subjected to long courses of treatment by radium, and especially by *x*-rays, sometimes developed a peculiar form of cachexia from which they died, although their tumors had remained quiescent or had practically disappeared. These patients presented anemia, emaciation, great weakness, persistent leucopenia and at times nervous instability with attacks of maniacal delirium.

I have studied at autopsy several cases of this type and found that the pathological conditions vary and depend largely on the nature of the original disease. The bone-marrow regularly exhibits a pronounced reduction in the blood-forming tissue, and that which remains is poor both in nucleated red cells and in white cells, and may show hemorrhages, pigmentation and mucinous degeneration. These changes fully account for the peculiar anemia. The spleen shows evidence of marked draining of white cells, atrophy of follicles and extensive destruction of red cells. A prominent element in the cachexia sometimes appears in

the extensive fibrosis which follows regression of the tumor tissue, which interferes with the circulation and function of affected organs. Thyroid atrophy, constriction of great vessels and chronic catarrhal enteritis may be found when the regions of these organs have been greatly exposed. Not infrequently the cachexia is found to be mainly referable to chronic infection, which is very readily established in the debilitated body.

Prolonged treatment of Hodgkin's granuloma usually terminates in very extensive sclerosis of many organs and complete loss of lymphoid tissue throughout the body. A careful general anatomical study is required to trace the factors concerned in various cases. Nevertheless, these observations indicate that there is a limit to the radiation that the human body can withstand. In planning the course of treatment in diseases of chronic course and generally unfavorable prognosis, one should endeavor to avoid too frequent and severe exposures, and should consider whether the patient will not live longer if treated on the expectant plan, prolonging the periods of improvement as much as possible and thus avoiding the addition of cachexia to the terminal stages of the disease. These considerations apply especially to Hodgkin's disease, leucemia and recurrent mammary cancer.

THE METHODS AND INDICATIONS FOR RADIATION THERAPY

The wisdom of employing radiation in cancer depends first of all on the competence and equipment of the operator. Current literature still reveals wide differences of opinion regarding both indications and methods in radiation therapy, and these differences are mainly dependent on the experience and technical equipment of the authors. Thus in Germany, and until lately in France, lingual cancer has regularly been classed as unsuitable for radiotherapy, an opinion due solely to the failure to employ radium needles in the tumor tissue. In Germany, *x*-rays have largely supplanted radium, so that German opinions are usually tempered by the limitations of the *x*-ray machine. On the one hand we find everywhere the opinions of those equipped only with radium or

x-rays or both, opposed to the views of surgeons who use neither or who have a little radium to use on occasions. Quite numerous are the beginners who are deficient in knowledge, experience and equipment and who work their way through stormy paths to various degrees of efficiency. The result is that there are no standard indications or methods in radiation therapy, except in a few minor conditions, and there probably will not be until some central authority establishes these standards and insists that radiologists shall meet them. The time seems to have arrived when a special license or diploma attesting the operator's competency should be required of all who engage in this work. Recognizing the great difficulties in the way of such regulation, many have concluded that the treatment of cancer by radiation should be mainly in the hands of large institutions fully equipped for the diagnosis and treatment of cancer in all its forms and by all approved methods. While endorsing such a plan, I must confess that it hardly does justice to the remarkable achievements of many surgeons who, with great skill and knowledge, but with limited equipment, have often been the pioneers of progress.

Under these circumstances the writer can only offer his own conclusions in this complicated field, which are based mainly on the work of his clinical colleagues at the Memorial Hospital, where radium, *x*-rays and surgery are employed in accordance with the judgment of the staff.

Lymphoid tumors offer the most impressive field for radiation therapy. It is now generally recognized that lymphosarcoma belongs exclusively to the radiologist, since the tumors yield rapidly to moderate dosage, and many localized growths never recur. It is highly important to avoid incision for diagnosis, since these tissues are very susceptible to infection and the scars break down under radiation. A discrete, movable node may be safely excised. In generalized systemic lesions the prognosis still remains unfavorable, owing to the wide extent of the disease, and there appear to be few cures of ulcerating lymphosarcoma of the intestine. Very striking initial results and a few apparently permanent regressions are observed with mediastinal lymphosarcomas, most of which belong with the thymic tumors.

Hodgkin's granuloma presents many problems. While the initial regressions are usually impressive, especially with early cellular lesions, the final results are generally disappointing. The disease recurs after a year or longer, sometimes promptly, and in a more resistant fibrous form, while the tendency toward extensions seems to be little affected. Overradiation leads to extensive fibrosis, anemia and cachexia supervene as usual and the total duration of life is not increased and may be shortened. On the other hand a small proportion of cases seem to be permanently relieved. Since thorough excision of Hodgkin's lymph-nodes is rather seldom followed by local recurrence, the indications for surgical interference and radiation in this disease seem not yet finally determined. One can fully endorse the warning given by Yates that overradiation disturbs the nutrition and blood-forming powers of the patient and tends to shorten life. It may well be that the best treatment of Hodgkin's disease is excision of all accessible enlarged lymph-nodes, with radiation for the deeper lesions.

Although radiation has proven to be the best treatment for leucemia, the same precautions against overdosage are required, and almost the same disappointments are experienced, as with Hodgkin's disease.

Embryonal Tumors in Children. A long list of embryonal tumors, many of which are difficult to classify, respond promptly to external radiation, which should always be employed before the resort to surgery. These tumors include Wilms' tumors of the kidney; teratoma of the ovary and the testis; glioma of the retina, brain and cord; neurocytoma; abdominal and mediastinal teratomas; myosarcoma of the prostate; polypoid cervical myosarcoma; pharyngeal myxosarcoma.

I know of no record of the treatment of chorionic carcinoma by radiation, but this is preeminently an embryonal tumor and should follow the rule with other embryonal growths.

Cutaneous Cancer. Radium treatment is indicated in all primary cancers of the skin and is successful in the great majority of uncomplicated cases.

Basal-cell carcinomas yield, as a rule, to surface applications of silver-filtered radium. An excellent and

expeditious method is the one- to two-minute exposure to large amounts (300 to 500 mc.) of emanation condensed in a small glass bulb and applied unfiltered, a method devised by Quick.

Squamous carcinoma is distinctly more refractory and generally dangerous. It may yield to surface applications, but often requires the caustic action of emanation needles. Bulky tumors may first be excavated by electric coagulation or other caustic and the base treated by needles. Very advanced cases, involving mucous membranes or bone, still carry a poor prognosis. Quiescent pigmented moles are better excised. Early melanoma should receive very heavy external radiation, which may be followed by wide excision, but the results are generally poor.

Cancer of the Lip. Although surgical results with labial cancer are excellent, radium accomplishes as much or more without mutilation. These lesions can generally be attacked from three sides by surface radiation, but when deeply infiltrating, emanation needles are usually indicated. All localized operable lesions ought to be destroyed by this method. At the Memorial Hospital during the last three years, since this technique was introduced, not a single early case has been lost, and many advanced cases are in the group of apparently cured.

Squamous Cancer of the Tongue and the Mouth. By the use of emanation needles inserted throughout the tumor after preliminary radiation, buccal cancer has been transformed from a very grave surgical problem into a comparatively simple and very successful field in radium therapy. The only failures should be inaccessible lesions beneath or behind the tongue, those that invade bone, and very advanced cases. Certain lesions of the cheek also prove refractory and destructive. By the same methods, cancer of the tonsil may be controlled when not too far advanced. To combat lymphatic invasion the radium pack or *x*-rays may be applied over both sides of the neck. If definite infection of nodes appears, the nodes may be excised, leaving radium needles in the bed. If the capsules of the nodes are invaded it is probably better to insert radium needles and not attempt excision. In fact, the writer is inclined to believe, on the evi-

dence available, that lymph-nodes invaded by squamous carcinoma should always be treated by radium needles, and usually without excision. In all advanced cases preliminary ligation of lingual or external carotid is a wise precaution, as most of the deaths result from hemorrhage. During the past three years, since the introduction of the proper technique, about 90 per cent of the so-called operable cancers of the tongue and the mouth have shown a complete clinical regression. Some of these will undoubtedly recur, but most recurrences develop within a few months and may respond to further treatment.

Mixed tumors of the salivary glands respond well to external use of radium and *x*-rays, which should be used by preference in all primary cases. Complicated cases present a wide variety of conditions, for which several expedients must be employed.

Cancer of the penis is a refractory form of squamous carcinoma, and it may be mentioned to illustrate the dependence of results on the anatomy of the organ affected. The thin epithelial covering of the glans is closely adherent to the heavy fibrous tunica which encloses the cavernous tissue. While long restrained by the tunica, squamous carcinoma once breaking through finds itself in a roomy system of vessels. The lymphatics leading from the glans are also rich and wide. Finally, the submucosa between the epithelium and the tunica is very thin and affords little opportunity for the cellular reaction following radiation. Accordingly, these carcinomas are difficult to eradicate, but with preoperative radiation, followed by amputation, the results are better than by amputation alone. Yet many early papillary tumors respond well to radium alone.

Uterine Cervical Cancer. Opinions regarding the best treatment of cervix carcinoma still vary widely and follow closely the technical skill, equipment and mental attitude of the operator.

Three anatomical forms of localized cervical cancer should be separated in dealing with this disease, and especially in planning treatment by radiation: (1) Fungating polypoid carcinoma of the portio vaginalis; (2) flat carcinoma of the cervical canal, often squamous; (3) deep-lying carcinomas of

the cervical tissues, which often invade the parametrium before they reach the mucous surface. The prognosis by all forms of treatment varies in the order named. Both surgery and radium should cure a high proportion of these localized lesions. However, really early localized cervical carcinoma is rarely encountered. The difficulty lies with lesions which appear to be localized but are really extensive, and which the surgeon leaves partly behind or disseminates, and the radiologist fails to reach. Thus far statistics seem to favor distinctly the use of radium by an aggressive technique in dealing with apparently localized cervical carcinoma. The technique includes the insertion of radium needles in all the palpable tumor tissue followed by heavy doses of filtered radium from the vaginal route and radium packs or high-voltage *x*-rays over the abdomen. By such treatment, Bailey finds that about 80 per cent of the cases classed as favorable experience a complete clinical regression. Radical surgery has never produced any such primary results, while the frequency and progress of recurrences after radiation are both probably less than after surgery. Under such circumstances little remains of the field for surgery in carcinoma of the cervix. In the group of inoperable cases radiation has now many complete clinical regressions and some five-year cures, besides palliation of a great number.

I have seen pronounced radium changes in cancer cells in deep iliac nodes receiving external radiation, but have never had opportunity to prove that external radiation can completely destroy such metastases. The most that can be reasonably hoped for is retardation of the process. Yet Perthes reports one case of cervical carcinoma completely cured by deep *x*-ray therapy, and the Germans seem to place great reliance on this method in dealing with this disease. From their reported results it would seem advisable to employ deep *x*-ray treatment in all cases in addition to the local treatment by radium.

Having failed to find any trace of carcinoma in several uteri which had been the seat of well-established cancers and were treated by radium as above outlined, I am not impressed by the wisdom of performing hysterectomy after radiation. Yet it cannot be denied that hysterectomy may

possibly eradicate some degenerating but viable foci of cancer cells which might later give rise to recurrence. It seems equally if not more capable of loosening and disseminating outlying cell groups which under heavy radiation would long remain harmless. Yet if the case cannot receive the full radiation in the most approved manner, and if the disease is not advanced, it is probably better to extirpate the uterus a few weeks after treatment.

It is evident that the correct choice of treatment of cervical carcinoma raises many problems which can only be solved by much careful clinical study by radiologists and surgeons using the best technique. The experience with the radiation of advanced cancer clearly calls for a reduction in the scope of operability in this disease in the practice of those who do not use radium.

The unexpected success of radium treatment of cervical carcinoma seems attributable to two main factors: (1) The cervical tissues form a resistant filter so that relatively large doses of radium can be inserted in the canal and in the tumor tissues. (2) The majority of cervical carcinomas resemble the basal-cell tumors and are more susceptible to radiation than squamous carcinoma. On the other hand, the inaccessibility of cervical carcinoma will always render it very difficult to extirpate this organ without disseminating tumor cells. These facts will probably assert themselves sooner or later in the final decision as to the choice of treatment of cancer of the cervix.

Corpus Carcinoma. This disease occurs in quite varied forms which present very different therapeutic problems: (1) A localized, fully developed, malignant adenoma covering a limited area in any part of the endometrium. (2) Diffuse adenocarcinoma involving the entire endometrium. (3) Diffuse adenocarcinoma of both endometrium and tubes. (4) A diffuse, superficial, partly developed adenocarcinoma, intermediate between hyperplastic endometritis and true carcinoma, of moderate malignancy and often curable by curettage. (5) Diffuse adenomyocarcinomatosis affecting both endometrium and myometrium. (6) Localized carcinoma arising in an adenomyoma.

Anyone who attempts to treat corpus carcinoma by radiation should endeavor to visualize the anatomical conditions

in these different types of the disease. The examination of curettings is only the first step in this undertaking.

The difficulties of determining the exact local condition and the considerable success of hysterectomy seem likely to render slow the progress of radiation therapy in this field. Hysterectomy should be preceded by radiation, while the superficial cases of moderate malignancy may be entrusted to radiation alone. As a rule, corpus carcinoma has been undertreated, and it should be realized that malignant adenoma is relatively resistant, requiring 4000 to 8000 mc. hrs. in the uterus. I have examined several uteri which had been treated by smaller dosage up to 3000 mc. hrs. and have found islands or diffuse areas of adenoma malignum which had remained quiescent but had survived over periods of one to four years.

Myoma Uteri. It has been abundantly shown that radiation produces a symptomatic cure in the great majority of uterine myomas, with reduction in the size of the tumor and relief of pressure and hemorrhage. Complete disappearance of the tumor is generally reserved for the small or medium-sized and softer growths. The hazards of sterilization have probably been overdrawn, but the danger of stirring up old pelvic infection is very real. The proper place of radiation treatment of myoma uteri will doubtless be determined in due time, according to clinical experience.

The recent analysis of this subject by Clark and Keene leaves little more to be said. Gellhorn also presents the indications for and results of radium treatment of uterine myoma from the most mature experience. Yet some observers believe that it is unnecessary to submit all these patients to an elaborate gynecological technique when they can often be cured by external treatment with radium or *x*-rays. Gauss and Friedrich report that about 75 per cent of the myomas they treat show complete disappearance with deep *x*-ray therapy. All the bad results that I have seen with the radiation treatment of myomas have occurred in cases in which the uterus was dilated, the mucosa curetted off and radium inserted into the cavity. This familiar procedure is not without some hazards, as it prolongs convalescence and converts the treatment into a substantial gynecological operation

which may not always be necessary. Before the days of radium I performed autopsies on the bodies of women who died from latent infection stirred up by simple exploration of the uterus or curettage.

The sophistry of using the alleged sarcomatous degeneration of myomas as a bar to radiation has been sharply rebuked by Clark. Radiation is probably the best treatment for sarcoma of the uterus. As for the small percentage of myomas associated with corpus carcinoma, it is assumed that competent gynecological examination precedes any treatment.

The steady and often rapid regressions of these large and rather cellular tumor masses are quite surprising and difficult to explain. The tumors undergo edematous softening and liquefaction with formation of cysts, or there may be widespread, simple necrosis with shrinkage and fibrosis. The result seems referable in part to the inhibition of ovarian function, but mainly to the sclerosis of blood-vessels, and often, as Gellhorn states, to direct injury of muscle cells.

Mammary Cancer. The radiation treatment of mammary cancer has been pursued much more seriously in France and Germany than in America. From Germany come several reports of complete eradication of the disease by deep roentgen therapy. While the primary results are often encouraging, I do not believe *x*-rays can be relied upon to effect a complete local regression except under very favorable conditions. Histological examination of mammary cancers heavily treated by *x*-rays reveals a series of striking changes with extensive destruction of tumor cells, but in the residual scar tissue some tumor cells in my material have usually survived. The combination of radium needles in the tumor and lymph-nodes with *x*-rays externally has been employed in France with encouraging success. This method employs the caustic action of radium, which seems to be required in most forms of glandular and desmoplastic carcinoma. Regaud considers this plan of treatment to be reliable, but in order to meet objections from the surgical side, would perform the standard operation afterward. At the Memorial Hospital, Lee reserves radiation for poor surgical risks, for women over seventy years of age, for malignant tumors in women under

thirty years of age, and for inoperable cases. The results seem to justify this plan for the present time. Some of the earliest cases treated in this way four years ago by Janeway remain well today.

Preliminary *x*-ray treatment has established itself with most observers as an indispensable preliminary to radical operation. Postoperative treatment is widely employed and enjoys a definite theoretical support, but its value is difficult to judge. It may destroy or render inert outlying foci or implanted cell groups. For inoperable cases systematic radiation prolongs life and reduces suffering in the majority of cases, but probably not in all, while there is no satisfactory evidence that it can completely eradicate the disease when it has passed the local lymphatics.

On account of the extremely variable anatomical and clinical characters of the disease, the difficulty of diagnosis, the danger of disseminating the disease by surgical manipulation, the extent of the radical operation and the frequency of recurrences, I believe that combined radiation therapy in the above form is destined to replace largely the surgery of mammary cancer. This problem must be worked out on selected cases over a long time period, and the answer seems likely to come from European sources before we in America are prepared to accept it.

Rectal Carcinoma seems to be sought by neither surgeon nor radiologist. The cases that reach the radiologist are usually advanced and complicated, and with them eradication of the disease is rare and palliation far from certain. The caustic action of radium is required with these adenocarcinomas, which usually excites much new connective-tissue growth. Quick employs radium needles in the tumor, in relatively high dosage, followed by extirpation of the involved area by electrocoagulation. More superficial lesions which have not passed the muscular coat should be amenable to the implantation of radium needles. I find no impressive statistical reports and no indications that the disease can be controlled by the high-voltage *x*-ray machine.

Tumors of Bone. I have elsewhere discussed at some length the radiation treatment of bone tumors, with the following conclusions:

Benign giant-cell tumors need not, as a rule, be incised for diagnosis nor curetted for treatment, since they yield characteristic radiographs and gradually recede when patiently treated by external radiation.

The round-cell tumors of bone regress rapidly under radiation, but the prognosis is generally poor because of multiple lesions and metastases.

Osteogenic sarcoma generally resists external radiation, but when this is combined with insertion of radium needles the progress of some tumors of this malignant class may be stopped.

Brain and Cord Tumors. External radiation controls the growth of many cellular tumors of brain and cord with relief of symptoms in many and with apparently permanent relief in a few. The skull is no serious bar to treatment and the normal tissues are resistant. The possibility of destroying many more brain tumors by exposure and the insertion of radium needles has never been submitted to a satisfactory test. There is a very urgent call for recognition of these facts by neurological surgeons. Frazier and Pancoast have made a substantial beginning in this field.

Prostatic cancer is best treated by insertion of radium needles within the tumor. Filtered radiation through the rectum and the urethra gives a slight additional effect where it is most needed. Bumpus would limit the rectal dosage to 600 mc. hrs. and the urethral dose to 400 mc. hrs. When the disease is confined within the capsule of the gland or its immediate vicinity this method should be successful, and clinical reports of a moderate number of successful cases support this belief. Yet very few cases of prostatic cancer are recognized in the early stage.

Carcinoma of the bladder has been successfully treated by Barringer, Young and others, by insertion of radium needles into the base of the tumor and the surrounding tissue. Fatal cystitis and suppurating nephritis are, however, rather frequent complications of this method, especially in cases with previous infection. The results are generally recognized as a distinct improvement over those secured by simple extirpation.

Tumors Not Now Amenable to Radiation. Melanoma is, most unfortunately, highly resistant to all forms of radiation,

which produces at most only temporary slowing of growth. In that form of the disease which tends to confine itself to lymph-nodes there may be some indication for inserting radium needles in the nodes, but the generalizing forms are not benefited. To remove a suspicious pigmented mole requires the caustic action of radium.

In epithelioma of the esophagus there is very little evidence that definite improvement in the lesion can be secured by surface application of radium. There are a few isolated reports of successful cases, but there is great danger of doing more harm than good by passing radium tubes into the esophagus. The very thin epithelial lining of the esophagus, its rich vascular and lymphatic connections, the proximity to vital structures and the rapidly invasive character of its epitheliomas indicate that cautious palliation is all that should be attempted.

Gastric Cancer. The inaccessible location, the anatomical conditions and the results thus far obtained do not encourage the hope that any technique will soon be devised capable of controlling this the most frequent form of cancer. I have seen one adenocarcinoma of the pylorus completely destroyed by radium needles inserted into the tumor from within, but the patient died in two weeks with uncontrollable vomiting. The radium dosage was much in excess of the need.

On the other hand, external radiation has produced some remarkable results in relieving stenosis and in restraining the growth of advanced cases. With diffuse carcinomas, external radiation combined with gastroenterostomy has a limited but important field. Since gastroenterostomy alone may be followed by much improvement in the patient's condition, the credit in some of these cases must be assigned with caution.

Neurosarcoma is strongly resistant to all forms of radiation. About 150 cases of this disease, mostly recurrent, have passed through the Memorial Hospital in the last three years, and usually without notable benefit. Persistent external radiation seems to have controlled a very few.

Epithelial tumors invading bone or arising within it, as adamantinoma, should be treated surgically, since severe

radiation of bone produces painful osteitis and generally fails to affect the tumor.

Carcinoma of the larynx, except in early intrinsic lesions, offers many difficult problems for both surgery and radiology, in which radium has furnished very limited aid. Quick's method of applying short exposures of large amounts of emanation compressed into a small glass bulb seems to have controlled some early intrinsic lesions.

THE INFLUENCE OF RADIATION THERAPY ON THE CANCER PROBLEM

Will the possession of new physical agents capable of controlling localized accessible cancer influence the general aspects of the cancer problem? Will the wide and efficient use of these agents affect the death-rate as shown by the United States Census, or will the benefits be confined to the comparatively few individuals who early visit the modern cancer clinic while the major portion of the sufferers continues to be sacrificed?

There are some reasons for believing that in due course of time the new therapy cooperating with and in some respects enlarging the old, and combining with the campaign for the early recognition of cancer, will actually decrease the recorded death-rate from cancer and thus attain very real economic importance. In the first place the actual five-year cures of several major forms of cancer, heretofore fatal, are now considerable in number and rapidly increasing. The fruits of improving technique are as yet hardly visible.

Then the prolongation of life in many cases only apparently cured gives opportunity for other causes of death to intervene and thus give a somewhat spurious diminution in the number of cancer deaths. The importance of this factor is not to be depreciated, as it represents a distinct step in advance.

Most important is the fact that radiotherapy is a bloodless method, and while not painless, it has no appreciable death-rate. Anyone who understands human nature cannot doubt that many more people will submit to radiotherapy than to the knife, and do it earlier. The treatment of many more sus-

picious or precancerous lesions will also be accomplished by the simple methods of radiation.

One serious obstacle stands in the way of prompt acceptance by the public of radiation treatment of early cancer and precancerous lesions, and this is the attitude of the medical profession toward the new therapy. It is, on the whole, a matter of congratulation that a method so revolutionary should have received such prompt recognition the world over. Only the most tangible and overwhelming evidence could have compelled this recognition. The rapid adoption of radiotherapy must stand as evidence of the intellectual honesty of the medical profession. Yet there is still an undercurrent of antagonism which reaches the public with much force, greatly impedes progress, interferes with the spread of knowledge, retards the acquisition of equipment and prevents many from receiving the benefits now available. For the same reasons probably, the practice of establishing radiation therapy in municipal hospitals, quite general in Europe, has been adopted in America only by the city of Philadelphia, where it has been established through the wise forethought of Dr. Furbush. Yet it appears quite inevitable that other cities must follow.

The policy of concentrating the care of cancer patients in large institutions, fully equipped for all the methods now demanded in diagnosis and treatment, also appears to be justified. It is probably the most effective method of avoiding the apprenticeship which beginners in this work must inevitably encounter. When by these various means and adjustments efficient radiation is fully available to the public and intelligently accepted, there is little doubt that the death-rate will be appreciably reduced.

The other phases of the cancer problem, however, remain unaffected by the new therapy. Extensive and advanced cancer will always be the discouraging problem of old. The need for a constitutional agent affecting the cancer process is still as urgent as ever, and apparently just as far from satisfaction. The task of unraveling the conditions of origin of the different forms of cancer, encumbered by the search for a single causative agent, has made little progress, but it may be stimulated by recent developments. From a most

unexpected source, experimental physics, a new and powerful weapon has been brought into play, cancer research has entered on a new and practically fruitful era of therapeutics and more intelligent descriptive study, new territory has been conquered, the outlook for the cancer patient is improving; but the ancient enemy still sits grimly in his stronghold.

INDEX

Andrews, 70, 81
Anschutz, 57
Arndt, 262

Bagg, 111, 129, 137
Bailey, 108, 129, 139, 279
Baisch, 83
Barlow, 170, 172
Barney, 224, 226
Barringer, 109, 174, 192
Bastianelli, 41, 42, 49, 72, 81
Bergonié, 246
Bertolotte, 57
Biopsies, 151
Bloodgood, 34, 35, 41, 71
Broders, 34, 35, 41, 71, 73, 81
Brown, 138
Bumpus, 177, 284
Burnam, 111
Butlin, 41, 42, 49, 69, 80

Caird, 42, 49
Cancer, 243
  corpus, 280
  cutaneous, 276
  epidermoid, 4
  gastric, 285
  intraoral, 69
  mammary, 282
  of bladder, 177, 192, 284
    breast, 3, 145
      primary inoperable, 150, 162
        operable, 149
      recurrent inoperable, 150, 153
    cervix, 108, 124, 278
    esophagus, 57
    female generative organs, 108
    floor of mouth, 60
    larynx, 3, 286
    lip, 32, 277
    maxilla, inferior, 62
      superior, 63

Cancer of mucosa of cheek, 61
penis, 278
prostate, 174, 284
rectum, 3, 82, 283
tongue, 41, 277
uterus, 123, 138, 278
vagina, 123, 129, 134
vulva, 123, 129, 131
radiation therapy in, 243
Canuyt, 57
Capetti, 42, 49
Capillary tubes, 6
Carcinoma. See *Cancer.*
Cervical lymphatics, 69
metastases, 80
Cesbron, 27
Chaoul, 265
Cheatle, 69
Clark, 281, 282
Clowes, 258
Cobb, 42, 49
Coley, 51
Concentration of scattered rays, 264
Crile, 69, 70, 80
Cystogram, 197

Dawbarn, 51
Dean, 213, 220
de Keating-Hart, 270
Dobson, 70, 73, 81
Dollinger, 34, 40
Downes, 185
Duane, 129, 250

Edling, 57
Ewing, 34, 40, 49, 72, 73, 81, 92, 157, 185, 188, 192, 193, 194, 213, 214, 242, 243
Eyeball, new growths of, 95

Failla, 5, 13, 24, 100, 114, 217, 263
Farrar, 49
Filtration, brass, 24
lead, 22
platinum, 25
silver, 22
Frazier, 284
Freudenthal, 57
Fricke, 34
Friedrich, 17, 281
Furbush, 287

Gant, 83, 92
Gauss, 281
Gaylord, 258
Gellhorn, 281, 282
Geraghty, 181
Gibson, 158
Goeller, 182
Goodale, 57
Goris, 57

Handley, 73
Harris, 57
Hartmann, 83, 92
Hartwell, 83, 92
Healy, 138
Herendeen, 167
Hertwig, 263
Hodgkin's granuloma, 274
Hoffman, 262

Inguinal adenopathy, 224
  lymph-nodes, 226

Jacobson, 41, 57
Jamieson, 70, 81
Janeway, 1, 5, 37, 41, 43, 52, 57, 87, 92, 130, 136, 137, 162, 213, 250, 283
Jess, 269
Jessett, 41
Joly, 129, 137
Jones, 82
Jungling, 264

Keene, 281
Kelly, 111
Kepler, 263
Keyes, 184, 185, 186, 213, 215
Kroenig, 17
Kupferberg, 270
Kuster, 76, 81

Lathrop, 42, 49
Lee, 145, 153, 160, 162, 282
Lusk, 83, 84, 92
Lymphosarcoma, 4
Lynch, 82, 83, 86, 92

Mallett, 110
Mandlebaum, 193
Matthews, 50, 57

Mayo, 83, 92
McCoy, 57
Meller, 41, 42, 71
Method of radium treatment, 198
Methods, of buried emanation, 26
  of radium application, 7
Mohan, 186
Morestin, 42, 49, 69, 71, 81
Mütter lecture, 243
Myoma uteri, 281

Neoplasms, intraoral, 80
  of the larynx, 66
Neurosarcoma, 285

Orbit, new growths of, 95

Pancoast, 284
Parotid gland, 93
Penis, epithelioma of, 220
Perrier, 52, 57
Perthes, 264, 279
Piquantin, 45
Poirier, 42, 49

Quick, 31, 57, 82, 93, 95, 97, 227, 250, 277, 283, 286
Quimby, 108, 118, 131, 137, 139

Radiation, 145, 162, 262
  measurement of, 115
  therapy, 243
    deep, 263
      adjuvants to, 269
    influence of, on knowledge of tumors, 270
      on the cancer problem, 286
    methods and indications for, 274
Radium, 138, 153, 192, 213
  active deposit, 6
  and roentgen rays, 153
  buried, 201
  emanation, 1, 5, 129
  therapy, 1, 5
  unfiltered, 19
Regaud, 27, 252, 282
Rennington, 82, 83, 92
Roentgen rays and radium, 153, 232
Ryall, 73, 81

Salivary glands, mixed tumors of, 278
Sans, 34, 40
Scannell, 42, 49
Schmitz, 17
Seitz, 264
Simmons, 42
Steiner, 34
Stevenson, 129, 137, 249
Stone, 126, 232
Suguira, 263
Sutherland, 221

Tribondeau, 246
Tumors, embryonal, in children, 276
  epithelial, invading bone, 285
  growth of, 261
  influence of radiation therapy on knowledge of, 270
  intraoral, 31, 65
  lymphoid, 275
  malignant, *x*-rays and radium in treatment of, 232
  not now amenable to radiation, 284
  of bone, 283
    brain, 284
    salivary glands, 278
    skin, 97
    tonsils, 49
  teratoid, of the testicle, 213
  treatment of, 232
Tuttle, 82

Von Bonsdorff, 34, 36, 41

Warren, 41, 70, 81
Watson, 57
Weigert, 257
Weil, 250
Werner, 264
Wetterer, 270
Wintz, 264

Yates, 276
Young, 284

Paul B. Hoeber, Inc., 67–69 East 59th St., New York

THE LIBRARY
UNIVERSITY OF CALIFORNIA
San Francisco

THIS BOOK IS DUE ON THE LAST DATE STAMPED BELOW

Books not returned on time are subject to fines according to the Library Lending Code.

Books not in demand may be renewed if application is made before expiration of loan period.

14 DAY
OCT 15 1982
RETURNED
OCT 13 1982

14 DAY
APR 28 1993

APR
1993
28 D
SEP 1 200

RETURNED
AUG 3 1 2006

15m-5,'70(N6489s4)4128-A33-9

598377

3 1378 00598 3773